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EPIDURAL HEMORRHAGE AND THE SKULL OF CHILDREN

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EPIDURAL hemorrhage in infants and children is said to be extremely rare. Thus, Peet and Munro and Maltby each report only 1 case in their personal experience while, in adults, Munro and Maltby find the incidence of epidural hemorrhages to be 3 per cent of all head injuries admitted to a large city hospital. Gurdjian and Webster, in a collective review of cases of epidural hemorrhage, found 2 cases (3, 13) resulting from birth injury and 5 cases in the childhood age period (6, 10, 22, 26). Four additional cases (17, 21) have since been reported.

The present paper reports 20 cases which occurred in a series of 1,136 consecutive head injuries admitted to The Children's Medical Center, of Boston, an incidence of 1.8 per cent. Although it is not proposed that the syndrome in children is essentially different from that in adults, no previous study has involved sufficient pediatric material to establish the usual clinical course in children. Included in the paper are anatomic data which were obtained in co-ordinated study of operative and postmortem material obtained from cases without cranial lesions.

MATERIALS AND METHODS

The normal anatomical features of the skull in children were studied in over 500 routine autopsies on children under the age of 12 years. The skulls were examined, usually from 6 to 12 hours postmortem, and particular attention was paid to the periosteum, skull bones of the vault and the dura. Sections were taken from the posterior portion of the right parietal bone in 22 patients at different age periods. The dural and periosteal connections were retained. Additional microscopic material was furnished by sections from bone flaps in approximately 100 operative cases. A large part of the autopsy material came from patients between the neonatal period and 2 years of age. The surgical material was mostly from patients older than 2 years.

Our clinical material consisted of 1,136 cases of head trauma hospitalized at The Children's Hospital, Boston, of which 20 were epidural hemorrhages. Only the cases of epidural hemorrhage will be analyzed. However, since the anatomical study proved to be of value in the consideration of the other cases as well, reference will be made to them during its presentation. The study will be divided into anatomical and clinical sections. The anatomical section will include a description of the layers overlying the brain, the changes in anatomy which occur during growth, the sources of bleeding in head injury, and the dynamics of clot propagation. The clinical section will present the physical findings, the progression of signs, the preoperative treatment, the operative technique, and the results. Short summaries of the case reports are appended.

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ANATOMICAL SECTION

It is common knowledge that the skull of the newborn is soft and elastic, that the wide sutures and fontanelles allow overlapping of bones in response to compression as well as facultative expansion, and that trauma to the head of infants tends to have less severe consequences than one ordinarily would expect. The protective mechanisms include the curved surface, the sliding skin and galea, and the mobile neck articulations, all of which tend to convert direct blows into glancing ones. With growth, all of these factors are altered, as well as the elasticity of individual fibrous and osseous elements, so that the pattern of rebound reaction of these elements varies exceedingly at different ages.

The layers of the skull to be considered are: the outer periosteum, the bone and the dura mater, which includes the internal periosteum. These three layers cannot be considered separately in explaining the effects of trauma because of their numerous fibrovascular interconnections which are more numerous in children than in adults, and which follow definite patterns changing with growth as will be described. Previous morphological studies of the skull of children are scanty. Other types of investigation of the response of the skull to trauma have been concerned almost exclusively with adult material. The data obtained in adults by stroboscopic, stresscoat, and similar techniques when applied to children require critical appraisal. In most reported experiments, the calvarium is usually separated from overlying and underlying membranes. This modifies the skull's physical characteristics, especially in the young where fibrous elements are so important a component. Further, these techniques, as well as experiments with animal material, mechanical models, and autopsy material do not take into account the variation in water content of living connective tissue elements which change during growth. A drying, dried, or fixed young tissue cannot react mechanically as will the living one. Finally, relative to extradural hematoma formation experimental techniques cannot counterfeit the vascular pressure factors acting long after trauma has occurred.

The variations with age in the reaction of the skull to injury may be attributed to 3 factors: first, the variable extent of the fibrous sutures and fontanelles; second, the existence of fibrous and osseous tissues whose morphology and elasticity coefficients change appreciably; and third, the differing degree of mechanical interdependence of the bony and soft tissue layers.

Our conception of the reaction of the skull to trauma is based upon morphological observations which are described below. The essence of our thesis is that juxtaposed layers of tissues, in response to trauma, expand or contract to different degrees, depending on the elasticity of their constituents. This difference results in a shear which becomes most significant where few fibrous connections exist between the layers. The investigation of the fibrous connections between the outer periosteum, the skull bones, and the dura shows that these connections are proportional in number to the rate of bone deposition, and conversely, are diminished at the areas of bone resorption.

The bones of the calvarium are membranous and their development is used in histology texts as an example of this type of bone formation. During the neonatal period, especially in the prematurely born, the bone deposition is very rapid. At birth, the bone present consists of a thin outer plate of fibrous bone of variable thickness underlaid by a thin layer of cancellous bone. The premature infant may have merely nodular flakes of fibrous bone (Fig. 1a). On the outer surface of this bone, lamellae are being deposited rapidly and therefore loosely, so that often the matrix and cell configurations appear cartilaginous. Besides these lamellae, new trabeculae form in the thick, rather loose periosteum, and are amalgamated into the bone beneath without perpendicular trabeculae being present (Fig. 1b). This incorporates substantial finger-like projections of fibrovascular periosteum into the bone structures and it is the tearing of these projections which gives rise to cephalhematomas. Because of the large number of these projections, little opportunity exists for massive collection of blood subperiosteally unless the trauma involves a large area (e.g., forceps trauma). Point trauma, as by striking

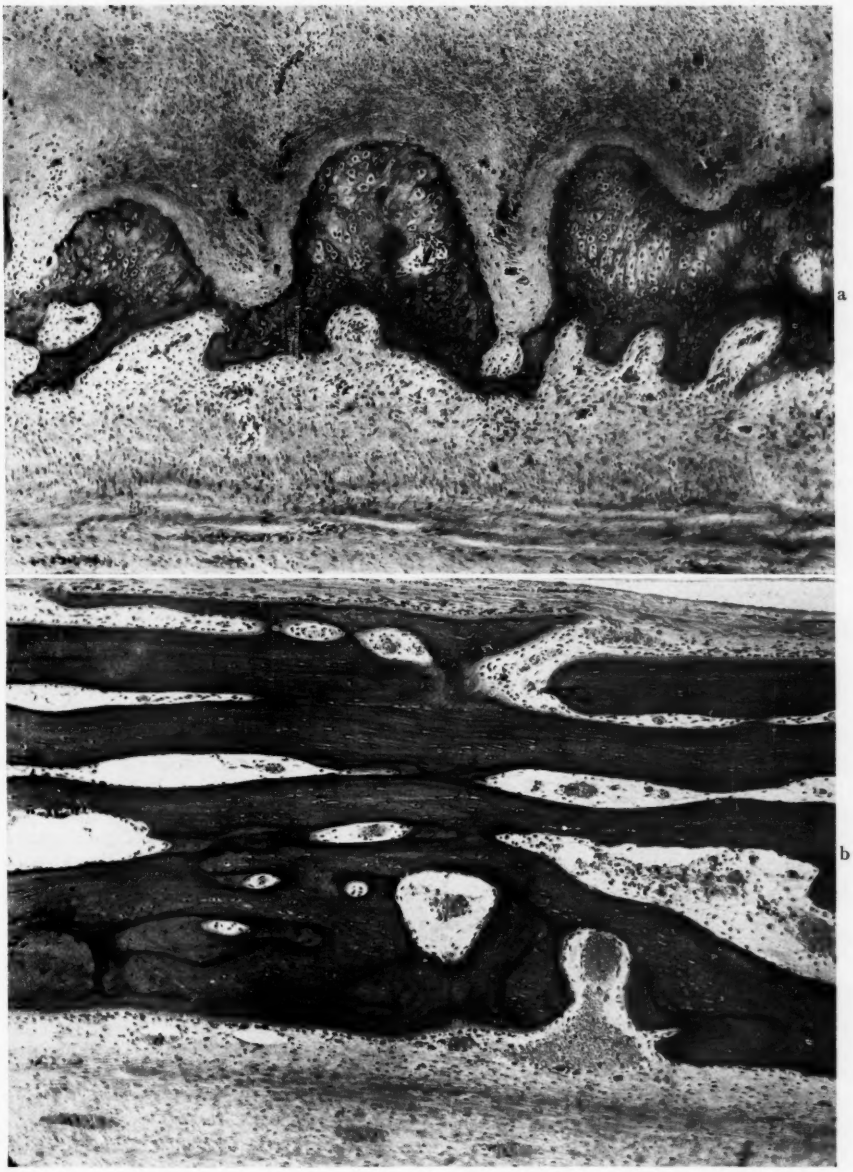

Fig. 1. a, Skull of infant born 2 months prematurely. Note thickness of periosteum, nodularity of the bony surface, rapidity of bony accretion on all bony surfaces. The layering of the dura is well shown. Note the beginning of a marrow space in the center. b, Skull of full term newborn. Note bony accretion on dural surface as well as periosteally. An adjoining area showed resorption on the dural surface. The mode of addition of osseous flakes to the periosteal surface is shown with a fibrovascular bridge centrally placed.

a sharp projection, usually raises a circumscribed area of periosteum by hemorrhage beneath it. The limit of extension of the collection of blood may be the nearby suture, at which point the periosteum is extremely adherent to the bone beneath by means of multitudinous Sharpey's fibers (Fig. 4). More often, a break in the periosteum allows subgaleal extension of the hemorrhage and significant quantities of blood may collect in the loose areolar layer—sufficient, sometimes, to bring on shock.

Outer periosteum. The evolution of a definitive periosteal membrane as is found after the age of 2 years, approximately, is demonstrable in histological examination of the infant skull. The periosteum early is a loose connective tissue layer with no definite orientation of fibers and with the fibrovascular projections mentioned above (Fig. 1b). Hemorrhage into this layer is more likely to permeate locally, and periosteal ecchymoses, indeed, are very frequently found postmortem in the skulls of the newborn. The looseness of the periosteal layer permits localized elevation of the cambium layer and, when this occurs, new bone may form over the clot, especially at its periphery. It is probable that the reason for peripheral bone formation in the cephalhematoma is in the more abundant blood supply to the region, while the supply to the dome of the lesion has been obstructed by trauma and tension. Subperiosteal hemorrhage in infancy may be conceived as the result of direct trauma by the active force on the periosteal vessels which are compressed against the bone beneath or sheared from it by a glancing blow.

The development of the periosteum from the period of infancy through childhood is marked by a progressive compacting of the tissues. The collagen fibers become coarser and longer and there are fewer cells and fewer vessels. Coincident with this change with age in the fibrous layer of the periosteum, the cambium layer lays down lamellae of appositional bone of maturer, more compact type, which results in a thick compact outer table (Fig. 2). The assumption by the periosteum of the character of a tough fibrous layer and the deceleration of bone deposition reduce the number of fibrous connections between periosteum and bone. This reduction accounts for the fact that with increasing age the periosteum of the calvarium strips somewhat more easily. During all of the childhood period, however, the attachment remains rather firm universally and is most firm at the suture lines where, despite cessation of growth, the attachment persists into adult life, tending to delimit subperiosteal hemorrhage provided the fibrous periosteum remains intact.

Bone. The formation of bone under the periosteum occurs at different rates in different localities. As a general rule, the portions adjacent to sutures are more active in bone formation than the central portions of bones during the first 2 years of life. At birth, the skull vault has a distinct outer table in nearly all of its extent, the expanse of the fibrous sutures excepted. The surface of this outer table is somewhat pitted and granular to gross examination. The pits correspond to the fingers of young fibrovascular periosteum communicating with the narrow interstices as described. The granules corresponded to the flakes of new bone being added appositionally. Beneath this outer table is a somewhat cancellous layer which constitutes, for the most part, the inner surface of the cranial vault. While many authors describe an internal table as existing at birth, we have found the structure definite only in the frontal area at the site of air sinus formation. Elsewhere, the distinction between inner tables and diploe seems insignificant for practical purposes. The significance of this anatomical arrangement in reference to fractures is obvious. Fractures in infancy tend to be linear and are very rarely comminuted. They tend to result from a creasing type of trauma and affect the whole skull thickness equally rather than showing the radiating fissures and depressions of the inner table as seen in adults. Only 3 of 12 fractures in our cases of epidural hemorrhage were comminuted. The inner surface varies greatly in its texture. It is roughened and shagreen at the centers of all 7 bones of the vault and is smoother at their periphery. At the points of roughening there is a paucity of fibrous attachments of the dura, mostly seen at the centers of the bones, while there is an abundance of fibrous attachments near the

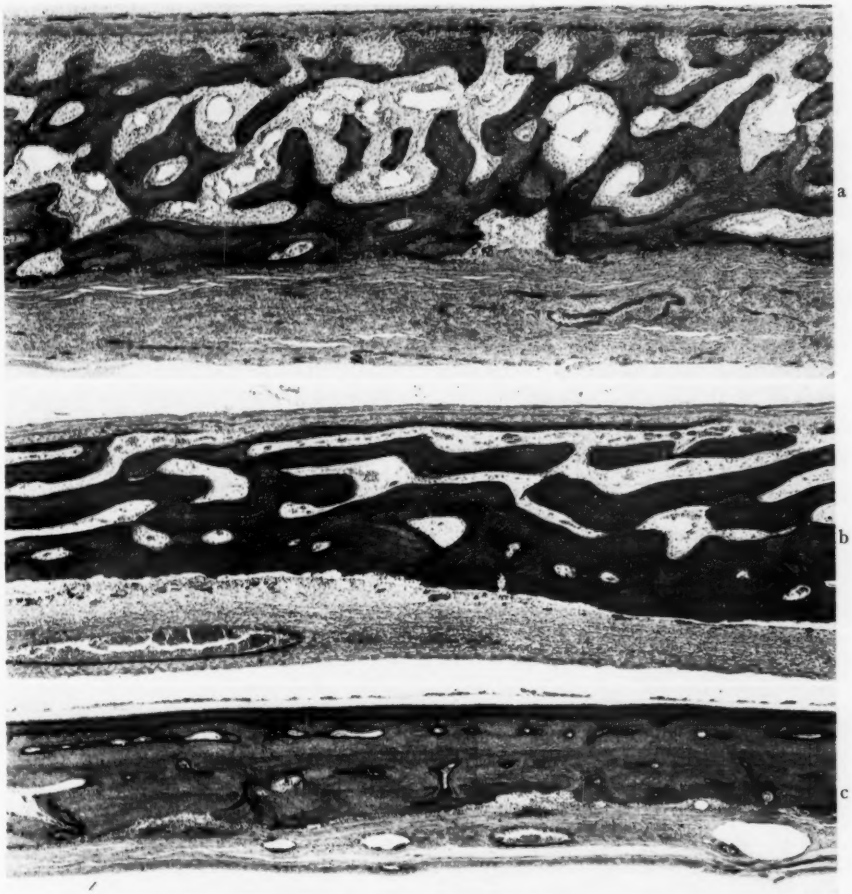

Fig. 2. Infant's skull, demonstrating bony resorption on the dural surface. The different patterns of bone architecture are shown. The fibrovascular tuft and distribution of vessels within the dura without protecting bony bulges as in the adult are also shown.

sutures. The distribution of these attachments permits the development of epidural spaces discussed below in relation to hemorrhage. Microscopically, the areas of smoothness consist of parallel lamellae of appositional bone, whereas the rougher central areas are areas of resorption (Fig. 2). The cancellous bone is lacy and its marrow is filled with young fibrous tissue which often contains hematopoietic foci. The areas of resorption frequently have osteoclasts apposing the bony spicules, but more often there can be recognized scalloping of the bony surface or cement lines which are at an angle to the surface (Fig. 2). At points of resorption, a looseness of the cellular tissue near the bone may occur so that often there is a narrow space next to the unicellular covering of the bone matrix. The bone matrix, itself, is very loose in texture and has larger numbers of osteocytes per unit area than does adult bone. Also, the haversian systems are rudimentary and cement lines are sometimes indistinct as befits fibrous bone.

The vault of the newborn skull not only varies in structural composition at different points, but also shows a great individual var-

iation at any one point. Thus, a newborn premature infant will show a much less coordinated structure at all locations than that given above. There are all gradations between the types of structure in Figures 1 and 2. Often in the matrix a darker blue-purple staining material with cells similar to chondrocytes in their capsule arrangement, may occur with superimposed osseous lamellae covering these at regions of bone formation (Fig. 4a). This tissue resembles cartilage matrix and is an example of the variability in the chemical composition of young bone, while also demonstrating the similarity it may assume, on staining, to other types of connective tissue, cartilaginous or fibrous. We believe that this type of supporting tissue is deposited when a very rapid period of growth occurs, and that the organization of tissues is too hurried for the usual type of matrix to be laid down.

The areas of the cranial vault in infancy which appear as digital impressions in the roentgenograms are characterized microscopically by thin plates of bone often resembling that shown in Figure 2 in which no cancellous bone can be made out at all. This merely confirms the wide variation in histological picture and offers difficulties in the mechanical theories of determination of skull curvature.

Further growth of the skull after the age of 2 years goes on at a much slower rate in accordance with the general deceleration of growth after the infancy period. At about this time a recognizable inner table is laid down which in all portions of the cranial vault consists of parallel lamellae. These are present along the greatest portion of all the calvarial surfaces and are not merely present in areas adjoining the sutures as in the earlier age group. Previously—that is, until the age of 2—well delineated tables were seen only in one location in the vault—the frontal region. The internal table is not deposited all at one stage of development but is added to at various periods and in various areas by slow and discontinuous accretion. Adjoining areas may show static and active phases as regards bone deposition. From the age of 2 years onward, there is a progressive patchy internal transformation of the bony elements so that the diploe become more prominent (Fig. 3). Trabeculae perpendicular to the tables appear and delimit the tables distinctly from the diploe.

Beyond the age of 7 years, when the skull circumference remains fairly constant, the histological character of the child's cranial vault differs little from that of the adult. What differences are present are those of texture, cellularity, and density of the elements rather than those of the pattern of structure. These differences, since they concern the elasticity coefficients of the layers, are of significance in the consideration of trauma to the bone.

Dura mater. The dura mater, the last of the layers covering the brain which will be discussed, shows marked differences incident upon growth and development. At birth it is thick and consists of a laminated layer in which three different components may be distinguished. The outermost of these is the inner periosteum of the skull. This is a loose cellular tissue which contains many thin-walled vessels. Much variation in the appearance of this layer depends upon whether osseous absorption or formation is occurring in the overlying bone. The layer is much looser and the vessels more dilated when resorption is taking place. The main meningeal arteries run between the periosteal layer and the fibrous layer to be described. The distribution of these arteries and their accompanying thin-walled veins is well described by Gurdjian and Webster. In the child up to the age of 5 years the meningeal grooves in the skull bone are quite shallow (Fig. 3) so that the principal factor protecting the vessel walls is the great elasticity of the vessel walls. Beneath the periosteum are two strata of dense connective tissue, the outer of these somewhat denser than the inner. The fibers of the outer stratum are parallel and it contains only a few vessels. The inner stratum, which is just outside the endothelium of the dura mater, is somewhat thicker and very slightly looser in structure. It contains many vessels, some veins, some arteries. Its fibers also run parallel but at an angle to the adjacent layer. Small veins are sometimes found at the interface between these two layers. As growth proceeds, all three layers become more and more compact and they also become thinner in each component. Along with the other components of the connective

Fig. 3. Skull sections at age 2, 4, and 8 years respectively. These sections show the alteration of pattern as the diploe becomes definite. Laminar accretion demonstrated by cement lines is shown at first to be mainly external and later to be both external and internal. The development of bony protection to the vessel is seen in these figures. The relative thinning of the dura relative to the bony layer is also shown.

tissues the fibers become coarser and there are fewer cells present.

Since during the development of the cranium the volume is increased, the curvatures of the bones of the vault are diminished, at first by resorption in some areas and later by differential apposition gradients (Figs. 2, 3). The areas affected most by resorption and later showing least bony apposition are those underneath the central portions of the frontal, parietal, and occipital areas. Because of the weakness of dural attachment at these sites which, we believe, results from these considerations, potential spaces are formed into which epidural hemorrhage may collect. Thus the subparietal space was the pocket in 4 of our cases, and the frontal space was occupied in 1 case. This confinement of hemorrhage would not be expected to occur where a fracture crosses the suture line.

Sutures. Most authorities agree that the fibrous sutures and their areas of widening, the fontanelles, are the main mechanism for the increase of areas of bones of the calvarium. At birth (Fig. 4a) the sutures are wide and loosely fibrous with many thin-walled vessels interspersed in the fibroblastic tissue. There is bony accretion occurring at the ends of the trabeculae bordering the suture. The fibrous elements are continuous across the suture from bone to bone. A few vessels may be seen to anastomose with those of the marrow but the majority of the vessels run within the sutural fibrous tissue perpendicular to the fibers. This may explain why hemorrhages from these vessels rarely occur as the result of birth trauma or molding.

With growth, the sutures become narrower in width and more extensive in depth and acquire digitations which are demonstrated in Figure 4b. The sites of the sutures are determined during the membranous stage of development of the fetal skull and the pattern of digitation of each individual suture also follows a predetermined specific plan as described by Thoma. By the age of 3 years these sutures, while still capable of demonstrable stretching (diastasis), as shown roentgenographically (Fig. 5), are narrowed in width sufficiently that appreciable movement cannot be elicited by manipulation. Throughout the pediatric age period this fibrous gap remains, and diastasis is therefore possible even though the interdigitations, which occur both in the vertical and in the horizontal plane, become more complex and tend to limit all motions to the minimum, except stretching. Stretching of the sutural fibrous tissue is in no way hampered by the interdigitation since no bony block exists to this direction of force.

The sutures persist as fibrous septa well into adult life and begin to be obliterated by bony union at the age of 22 years (14).

Sources of hemorrhage. The sources of hemorrhage into the extradural spaces are the arterial and venous channels of the dura. The arterial vessels are numerous and, accompanied by weak-walled veins, usually occupy shallow grooves in the skull after the age of 2 years. The arborization is extensive as is the anastomosis with the haversian vessels. They are the source of dural and bony ooze during operative procedures and may contribute to epidural hemorrhage when the dura is sprung free from the bone by trauma.

It is usually postulated that the source of hemorrhage is one of the meningeal arteries, which is especially vulnerable if a fracture line crosses its course. Four of our cases showed main branch middle meningeal hemorrhage, while 9 bled from posterior branch. In 8 cases no fracture was seen by x-ray or at operation.

The possible venous sources of bleeding are the veins accompanying, and often external to, the meningeal arteries (Fig. 3), the venous clefts within the dura into which run some small diploic emissary veins, and the dural sinuses which are the major avenues of blood outflow. Jones suggests venous bleeding as a possible primary source and certainly a secondary source of extradural hemorrhage, and he points out that since the vascular grooves in the temporal bones enlarge distal to the foramen spinosum, the grooves probably are made by the veins rather than the accompanying arteries. We have verified these anatomical studies, as also have Verbrugghen, McKenzie, Munro and Maltby, Reichert and Morrissey, and Voris.

Whether the bleeding be arterial or venous, it is doubtlessly initiated by the traumatic compression on the surface struck or by ex-

Fig. 4. a, Skull suture and adjoining bone at birth. The suture alone would fill the entire field. The mode of bony growth at the suture line is shown. The continuity of periosteum, suture, and dura is shown. The structure of the bone in the darker more cellular areas is chondroid and the matrix here stains bluish purple. b, Skull suture at 8 years of age. This section shows the interlacing digitations in the coronal plane and the rapid bony accretion at the suture line.

pansion on the opposite side (19). However, the pattern of compression is altered in children by differences in structure and elasticity. We agree with Bell that "dura mater is shaken from the skull at the part struck." He showed that when the skull is struck by a mallet blow

with force sufficient to "shake" loose the dura and then dye is injected into the carotid artery, the dye collects in the extradural space. We express the thought somewhat differently in terms of different coefficients of elasticity of dura and bone causing a shearing stress at the junction of the layers. Thus we may explain hemorrhage without fracture. Also, when the fracture is present, the dura remains intact, having been sheared loose before the bending of the bone resulted in fracture. In our cases, 10 showed no tear of the dura despite fracture. When long sharp spicules of bone are depressed by the fracture trauma, these may perforate the dura rather than tear it. One of our cases shows this phenomenon. Long tears of the dura, as by stretching or incision by infolding bone, are rare (1 case).

The trauma which initiates extradural hemorrhage may also produce tears in any of the tissue components in the area with significant effect upon the epidural hemorrhage. Thus, if the bony plate and its periosteum are ruptured, a vent may be provided for escape of the epidural clot into the subgaleal space. Or, if the outer periosteum remains intact, the extravasation of blood may form a subperiosteal hematoma.

Subdural bleeding in the absence of cortical laceration is usually the result of tears of bridging veins from the arachnoid to the dura and may accompany epidural hemorrhage when there is a rupture of one of these veins in addition to the dural separation. Tears of the dura in the absence of fractures are excessively rare (none in this series) and therefore subdural drainage of an epidural hemorrhage may not be expected.

DYNAMICS OF PROPAGATION OF THE CLOT WITHIN THE EXTRADURAL SPACE

The rate of propagation of the clot will depend upon the area of dura detached from the inner table of the skull by the blow, and the caliber of the blood vessels lacerated, be they arterial or venous. The incipient hemorrhage itself places an increasing and unrelenting tension on the remaining dural vascular and fibrous attachments. O'Connell points out that there is an average fluctuation of 80 millimeters of mercury in the cerebral intraventricular pressure within the pulse. This permits intermittent systolic enlargement of the hemorrhage, which tends to be tamped by the rise in cerebral intraventricular pressure accompanying systole and inspiration. This repeated fluctuating assault upon the thin walls and fibrous attachments of the blood vessels may cause their rupture, with further bleeding.

CLINICAL SECTION

The classic syndrome in adults of acute extradural hematoma formation is characterized by instantaneous loss of consciousness at the time of head trauma followed by rapid full recovery. A lucid interval exists for a variable period, until the onset of clouding of the sensorium which advances to coma. The secondary loss of consciousness, as McKenzie emphasizes, is usually associated with progressive neurological, circulatory, and respiratory signs caused by accumulative compression by the hemorrhage. There is usually a linear fracture present which traverses the meningeal grooves or the site of a dural sinus.

Age and sex incidence. In this series, just over one-half of the patients are infants under 25 months of age, the remainder are evenly distributed up to the age of 12 years (Fig. 6). It is clear that cases occur relatively frequently in infancy inasmuch as the vast majority of our patients with head injuries were over 2 years of age. The explanation of the incidence lies in the dural attachments, as described, which are weakest in infancy and in the vulnerability of dilated vessels at points of bony resorption. The incidence of this injury in males is double that in females in both the infant and older groups.

Physical signs. The common physical findings are shown in Figure 7. The *state of consciousness* will be described under progression of signs. *Swelling of the scalp* is not constantly present, but it is the most common sign. It marked the site of a fracture in all but 1 patient with fracture (Case 17) and marked diastasis without fracture in 1 other (Case 12). *Hemiparesis* occurred thirteen times in the series. A *Babinski sign* was observed nine times. This sign indicates incipient herniation of the temporal lobe through the tentorial

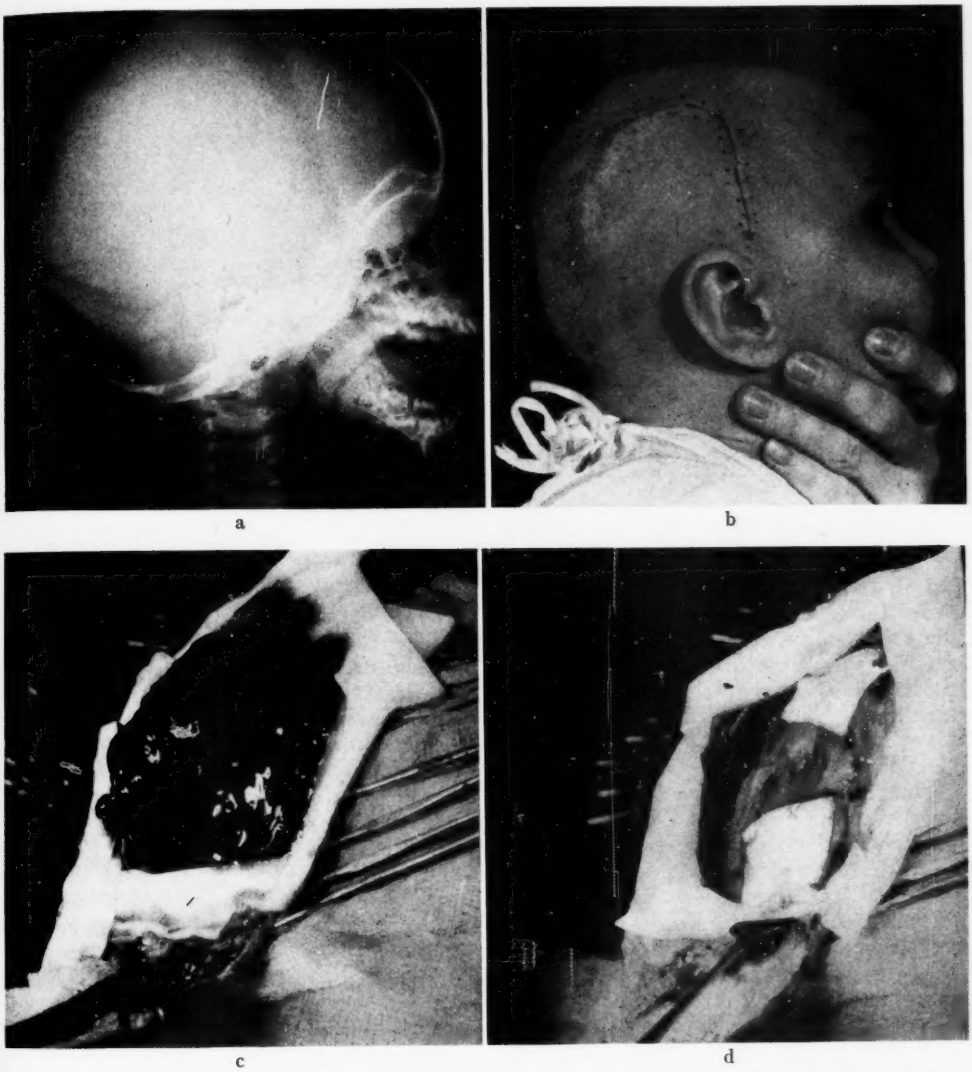

Fig. 5. a, Roentgenogram of Case 8, showing suture characteristics. b, Photograph showing scar to illustrate incision, Case 14. c, Showing epidural clot on exposure, Case 8. d, Showing cavity in Case 8 after removal of clot. The thickness of the clot is well shown. The cortex rapidly expanded to fill this space.

notch as Reid and Cone have pointed out. *Decerebrate posture* occurred five times, always in patients in coma who, at the same time, manifested circulatory and respiratory signs indicating medullary involvement. We view this sign as most ominous. One of the two fatalities in the series (Case 1) had this sign, while another (Case 13) was the only patient with permanent sequelae. Jefferson suggested that in man this pathological postural pattern may arise from the release of midbrain inhibition by the higher centers. Uncommon signs

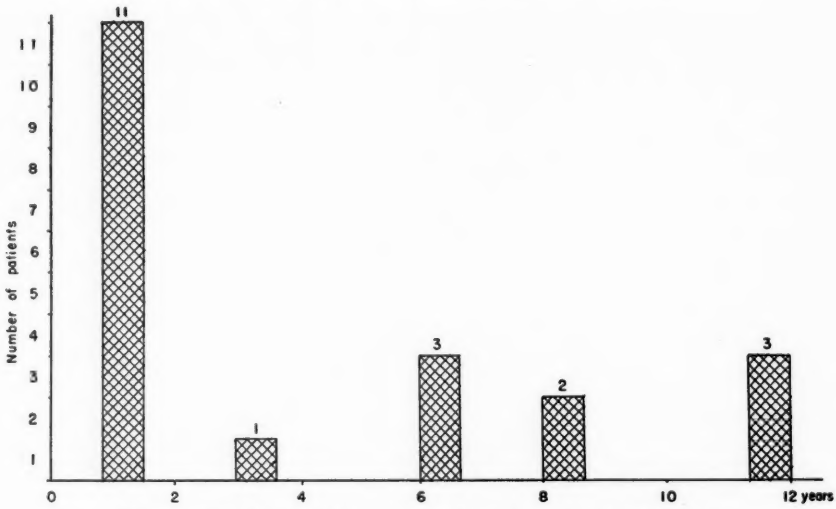

Fig. 6. Chart of age incidence, of 20 patients, 14 were males, 6 females.

are *papilledema* (Case 7), *strabismus* (Cases 5 and 8), and *convulsions*. The last occurred in 2 infants (Cases 4 and 8) both of whom survived without sequelae. *Stupor* and *coma* are common and occurred in 13 and 10 patients respectively. *Inequality of the pupils* with dilatation on the ipsilateral side was found in 9 patients, while 1 showed contralateral dilatation. They will be discussed further.

Repeated examinations of the temperature, blood pressure, pulse, and respiration are routinely performed. In 7 patients in this series, the *temperature* was under 98.6 degrees rectally soon after the injury, and this finding is a valuable indication of a serious lesion. The systolic *blood pressure* in this series showed no elevations characteristic of increased intracranial pressure as in the adult but 11 cases showed pulse pressures over 50. Allen-Williams demonstrated that the blood pressure in children up to 5 years should not exceed 99/66. The blood pressure of the children in this series was not a reliable indicator of the degree of shock. The respiratory rate of the patients in this series was not elevated or depressed significantly but a stertorous or sighing *quality of respiration* often indicated medullary involvement. The *pulse rate* exceeded 150 in only 4 patients under 5 years of age which was indicative of shock in view of the investigations of Allen-Williams, who showed that the resting pulse rate in this age group should average 110 and not exceed 150. A bradycardia of 80 or less in 8 patients was of diagnostic significance indicating increased intracranial pressure (Fig. 8).

Laboratory data. Lumbar puncture was carried out unless contraindicated by shock, or by increasing lateralizing signs of intracranial hemorrhage. The latter precaution is necessary to avoid herniation of the temporal lobe through the tentorial notch (Case 1). Thirteen patients in this series were subjected to lumbar puncture and clear acellular fluid was obtained in 9. Four fluids contained appreciable numbers of erythrocytes. The pressure in 6 patients ranged between 230 and 450 millimeters of water, while in 4 patients it was normal. Three patients had no manometric readings recorded. One patient (Case 8) was suspected of sepsis since his fluid contained 100 leucocytes per cubic millimeter in addition to 4,000 erythrocytes, and was under a pressure of 300 millimeters of water. After repeated negative cultures and prolonged observation, ventriculography was carried out and then a clot was removed operatively 11 days after the injury.

Anemia was evident in 4 patients in this series with erythrocyte counts ranging be-

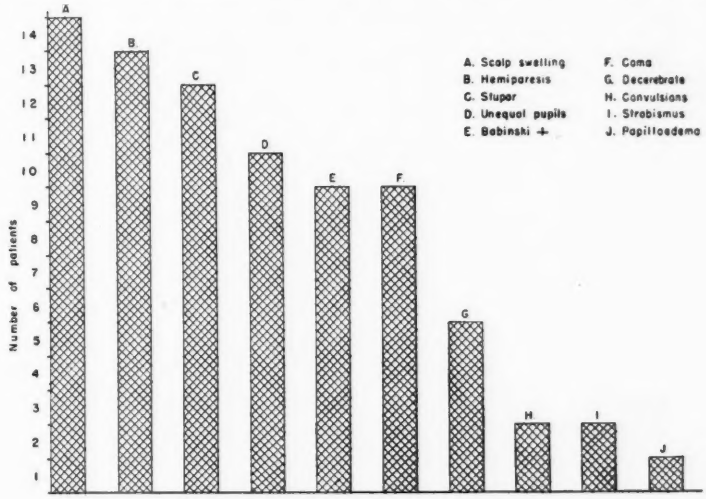

Fig. 7. Chart of common physical findings.

tween 2.1 and 3.7 million per cubic millimeter with corresponding hemoglobin levels. These patients were all infants and presumably normal prior to injury. We therefore suspect intracranial bleeding in any infant with a history of head injury who shows anemia, suspicion of other sources of bleeding having been eliminated.

Roentgenographic examination of the skull in this series of patients was performed in 17 instances (Fig. 9). Fracture was demonstrated in 11 patients, and diastasis in 10. Operatively, in the patients without roentgenography 1 patient (Case 14) showed a fracture with suture diastasis while another (Case 15) had only a diastasis. Of 8 patients without a fracture demonstrable roentgenographically or operatively, 3 patients presented suture diastasis roentgenographically. Only urgent necessity for blood replacement and operative relief of pressure are deemed valid contraindication to roentgenography. Thus in Case 1 patient was operated upon in a respirator, and in Cases 14 and 15 patients showed rapid progression of signs and accordingly no roentgenograms were taken.

The fracture was nearly always linear and either crossed the suture line or ended there. Often it ran across the grooves of the posterior or middle meningeal arteries, or both. Depression of one side of the fracture was an infrequent observation.

Progression of signs. Changes in the level of consciousness from drowsiness through stupor to coma frequently accompanied extradural hemorrhage in this series. The classic *lucid interval* after initial unconsciousness occurred in only 3 cases, while 1 patient (Case 2) with complicating cerebral laceration, did not recover from immediate posttraumatic unconsciousness. The remainder of our patients, 16 in number, did not suffer initial unconsciousness but were subject, after a *latent period*, to a progression of signs. The latent period varied from 15 minutes to 7 days (Fig. 8). Most lucid intervals or latent periods were shorter than 3 hours in duration and the shortest ones occurred where tributaries of the dural sinuses were torn. In addition to the deepening stupor, other signs may be progressive. A localized weakness may become paralysis, decerebrate posturing may become evident, or a pupil may dilate increasingly. Previously normal reflexes may become pathological, or convulsions may occur. A progressive fall in pulse rate and rise in blood pressure, changes associated with increasing intracranial pressure, in our cases were not always reliable indices perhaps because of opposite trends attributable to blood loss. Shock, therefore,

Number of case	Lucid or latent interval	Location of clot Fracture —— Diastasis ~~~	Age Years	Bleeding points	Pulse rate	Blood pressure	Remarks
4	7 days		0–1/12	?	—	—	Birth injury
14	1½ hours		0–7/12	Posterior meningeal	Rapid	90/40	Rapid progression, no roentgenograms taken
8	3 hours		0–9/12	Venous ooze	Normal	110/58	Anomalous spinal fluid findings. Operation delayed
11	2 hours		1–0/12	Posterior meningeal	Slow	86/52	Clot limited by suture lines
12	¾ hour		1–0/12	Posterior meningeal	Slow	114/35	Transient dilatation of contralateral pupil
16	1 hour		1–1/12	Posterior meningeal	Normal	110/80	Clot limited by suture lines
20	3 hours		1–2/12	Posterior meningeal	Rapid	110/60	Clot confined to 2 compartments by suture
5	15 hours		1–9/12	Tributary lateral sinus	Rapid	110/50	Transient decerebrate episodes
18	½ hour		1–10/12	Posterior meningeal	Normal	100/70	Sudden onset of decerebration
2	0		1–11/12	Tributary superior sagittal sinus	Slow	90/35	After 30 hrs. coma, ?? lucid momentarily, fatal outcome

Fig. 8. Clinical data.

Number of case	Lucid or latent interval	Location of clot Fracture —— Diastasis ~~~	Age Years	Bleeding points	Pulse rate	Blood pressure	Remarks
3	2 hours		2–1/12	?	Rapid	100/45	Lucid interval
13	1 hour		3–3/12	Posterior meningeal and middle meningeal	Rapid	110/60	Mild hemiparesis as sequela
9	½ hour		6–5/12	?	Normal	106/80	Progression of signs despite cessation of bleeding
19	1 hour		6–6/12	Posterior meningeal	Normal	115/75	No localizing signs
1	2¼ hours		6–7/12	Middle meningeal	—	70/00	Lucid interval, fatal outcome
7	24 hours		8–2/12	Venous ooze	Slow	100/60	Progression of signs despite cessation of bleeding
6	96 hours		8–6/12	Venous ooze	Slow	100/40	Clot limited by suture lines
15	¼ hour		10–11/12	Tributary lateral sinus and posterior meningeal	Slow	110/60	Rapid progression, no roentgenograms taken
10	6 days		11–0/12	Middle meningeal	Slow	124/70	Lucid interval
17	1½ hours		12–0/12	Middle meningeal	Normal	110/75	Fulminating progress, major vessel injury

Fig. 8.

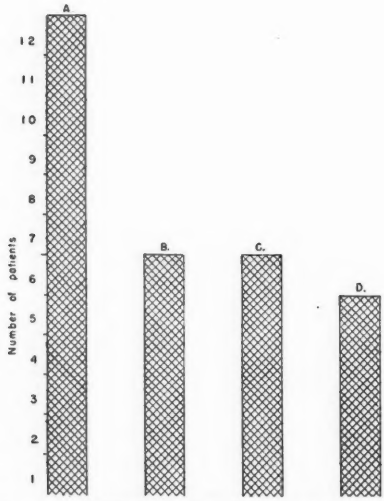

Fig. 9. Roentgenographic findings. Incidence of skull fracture and suture diastasis. A, Fracture; B, diastasis with fracture; C, diastasis without fracture; D, no fracture by roentgenogram or at operation; no preoperative roentgenography 3 patients.

was better ascertainable by the gray color of the face and the cold sweating skin. Coma supervened in 8 cases, including the 3 patients with lucid intervals and even in comatose patients a progression of neurologic signs sometimes occurred (Cases 18 and 20).

The rate of the progression of signs was largely dependent upon which vessel or vessels were lacerated (Fig. 10). The middle meningeal artery or a large venous sinus tributary produced a more rapid progression than did minor venous sources. The pliability of the skulls of infants and children provided by fontanelles or unfused suture lines and any immediate diastasis of the suture or fracture line may provide space for the accumulation of the clot. This mechanical factor may form the background of the long lucid intervals seen in some patients, but secondary bleeding or swelling of the clot by osmotic processes may also be significant. If the rate of accumulation of clot exceeds the compensating increase in cranial volume produced by the pliable calvarium, increasing compression of the brain occurs. First the cortical and then the medullary cardiovascular centers are unable to contend with the physiologic disturbances secondary to tension of first local and then generalized pressure.

Cerebrovascular collapse at the end of a long respite of accommodation constitutes just as much of an emergency as it does after a short one. Operation may be deferred if necessary upon a patient whose extradural bleeding has a vent into the subgaleal space via a marked diastasis of the fracture line. Then the outer periosteal vessel, as well as the diploic circulation adds to the hemorrhage, and the subgaleal blood collection may greatly exceed the extradural. The bleeding may amount to 200 to 400 cubic centimeters. If the patient is an infant or small child, this degree of blood loss may lead to profound shock if not promptly replaced. Where signs are not rapidly progressive, after several days of recovery from the almost invariable associated cerebral injury, operative removal of the clot, subgaleal and extradural, may be undertaken with a decreased mortality rate. Such hematomas involving the subgaleal as well as the extradural space are not infrequent. It is possible that this may partially account for the difference in incidence of acute extradural hematoma formation—1.8 per cent in this series of 1,136 head injury cases, versus 3.3 per cent in Munro's clinic.

If the full traumatic force is not spent upon the skull and dura, the least degree of cerebral injury, concussion, will occur and its mechanism will be compression or acceleration in type, depending upon whether the head is fixed or in motion when the blow is sustained. The unspent force may further cause cerebral contusion, laceration, subdural or intracortical hematoma formation. This is well illustrated in the laboratory work of Denny-Brown and Russell. All of these conditions, except simple concussion, are usually accompanied by skull fractures, localizing neurologic signs, increased intracranial pressure, and varying numbers of red blood cells in the cerebrospinal fluid. These signs also occur in associated or solitary extradural hematoma formations. The most valuable guide in detecting the last condition, whether or not one of the others is present, is an increase in lateralizing neurologic signs with concomitant increase in intracranial pressure. The differen-

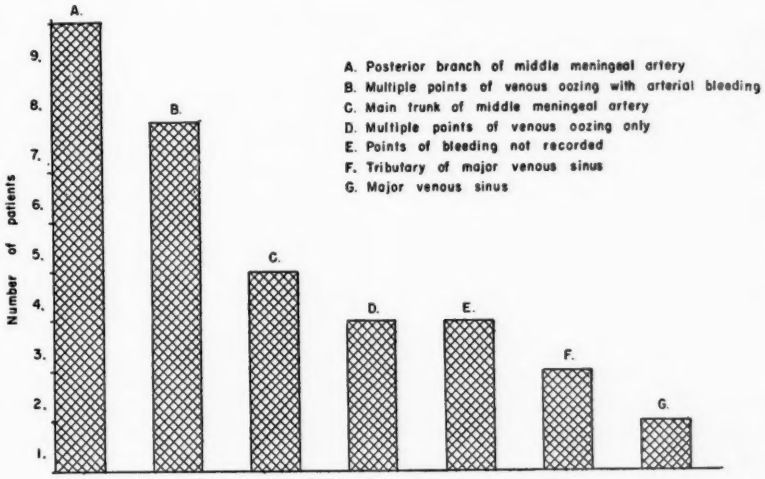

Fig. 10. Bleeding points identified at operation.

tial diagnosis is far from easy and can be confirmed with assurity only by burr holes. With increasing signs, trephination to determine the presence or absence of an extradural clot is indicated. Because an extradural hematoma can be simulated by many of the conditions mentioned above, a surgeon must not be disappointed by negative trephine openings on many occasions.

PREOPERATIVE CONSIDERATIONS

In the admitting room, an appraisal is made of the patient and of his history; his status is immediately determined in regard to shock and the gravity of his injury. If shock is present, the patient's blood is cross matched with blood available in the blood bank while the saphenous vein is being cannulated through a cut-down incision. We have found the pliable polyethylene tubing (11) more satisfactory than rigid metal cannulas where rapid blood replacement is necessary, inasmuch as it is less apt to be dislodged or become obstructed. During preparation for transfusion a complete history is elicited and physical examination carried out especially with regard to detecting possible coexisting visceral or skeletal injury.

By this time a tentative or probable diagnosis of extradural hemorrhage has been made as well as an estimate of the rate of progression of signs. In cases in which the signs are only slowly progressive, roentgenography may be helpful in diagnosing the site of injury, fracture, or diastasis. This diagnostic measure may be omitted if the signs are fulminant, when immediate operation is necessary. Then the palpation of a swelling and the presence of an ecchymosis seen upon shaving the scalp may be an accurate guide to the site of injury. Lumbar puncture may be done for diagnostic purposes only if lateralizing hemiparesis or unequal pupils or decerebrate posture are not present. Puncture may reveal evidence of coexistent subarachnoid bleeding. However, this diagnostic measure may also be omitted in case the progression of signs warrants such omission.

If the diagnosis is still in doubt or if the patient's condition remains relatively stable, a period of clinical observation may be in order. This should include a complete blood count, and frequent blood pressure, pulse, respiration, and temperature estimations. Delay may likewise be permissible if shock treatment is successful and no progression of signs occurs. A widely diastatic fracture line is good evidence that an exhaust vent for intracranial hemorrhage exists and patients exhibiting this sign may respond well to transfusion during the time that clot is accumulating in the subgaleal space.

OPERATIVE PROCEDURE

Premedication with atropine is desirable and the head, if not already shaved, is completely shaved with an electric razor after preliminary clipping with an electric clipper. Skin preparation with suitable antiseptics is followed by draping of a field of sufficient extent to allow exploration from the occiput to the frontal region and from the foramen spinosum to beyond the superior sagittal sinus. None of our patients have required external carotid ligations, but preparations for this contingency are advisable.

The anesthesia used is local procaine, ½ per cent with epinephrine added, supplemented by open drop ether if necessary. An initial subtemporal burr hole is made on the suspected side, and if a clot is encountered, the opening is enlarged anteriorly or posteriorly as indicated. In preference to enlarging the decompression, a bone flap may be turned anteriorly or posteriorly if needed, by means of a heavy scissors in the small infants or a de Vilbliss rongeur in the older ones. This method, where feasible, is more rapid than the use of the Gigli saw and affords easy access to otherwise inaccessible bleeding points. Replacement of the bone flap, after the bleeding is controlled, will avoid subsequent deformity of the skull.

If the bleeding point is arterial, a tantalum or silver clip is used for hemostasis or a silk suture may suffice. Venous bleeding is controlled by clips, coagulation, or absorbable hemostatic agents. The dura is now opened to determine if subdural hemorrhage or cortical damage has occurred. This step may be omitted if the dura is quite transparent. A drain is placed down to the dura if the brain does not fully expand after removal of the clot. It is left *in situ* for 12 hours. It has not been necessary in this series to establish a dural decompression unless there has been severe cortical damage.

If no clot is discovered by the initial subtemporal trephination, additional burr holes are made in the frontal and posterior parietal regions and then on contralateral side similarly. Closure with silk has been our custom.

During the operation parenteral fluids and blood are given, as indicated, through the saphenous cannula which has been kept open.

POSTOPERATIVE CARE

The blood pressure, pulse, and respirations are closely followed during the postoperative recovery period and furnish the best gauge of changes in the intracranial pressure. Determinations should be made frequently during the first 2 or 3 days, or longer if necessary. Lumbar puncture may be done daily if the original fluid revealed red blood cells and increased pressure. Customarily the pressure is reduced by half. Taps are continued until the red cell count of the fluid falls below 500 per cubic millimeter. Spinal tap is also performed as necessary when changes in signs or hyperthermia may indicate an increase in pressure.

When a drain has been inserted, sulfadiazine and penicillin are administered for 48 hours. Aspirin, phenobarbital or paraldehyde provide sufficient analgesia and sedation in these children; opiates are avoided because of their depression of respiration. Fluids are given by mouth or parenterally as required.

On several occasions it was thought necessary, because of continued elevated intracranial pressure, to explore on the contralateral side after primary evacuation of an extradural clot but in no case was an additional hemorrhage uncovered. Hence greater conservatism is used in postoperative interference; often careful observation for a few days will allow the cerebral edema to subside fully.

RESULTS

Usually complete return to normal is quickly attained postoperatively often within a few hours after recovery from the anesthetic. In 2 cases in our series, Cases 1 and 2, patients died after operation. The first patient was decerebrate on admission, and had been comatose for 2½ hours. A spinal tap, nevertheless, was done which we now deem to have been an error. Apnea followed and despite maintenance in a respirator and operative evacuation of the clot and tying of the bleeding point, the child never regained consciousness. The other fatality, also an early case, had a biparietal fracture with laceration of the superior longitudinal sinus. Despite supportive therapy for 3 days and then evacuation of the

clot, neurocirculatory decompensation occurred 16 hours postoperatively and death ensued. Autopsy disclosed subdural hematoma and brain laceration in addition to thrombosis of the lacerated sinus.

The only other patient (Case 13) in whom operative treatment had not been followed by complete recovery and normal development, has been followed 2 years, during which time he has shown a mild hemiparesis on the contralateral side, which is improving. He had transient decerebration on admission to the hospital but otherwise did not differ in his clinical findings from many others in this series. Since operation he has had one convulsion but has been mentally alert.

Reasons were sought during our study to explain the obvious discrepancy between the number of patients with epidural hemorrhage in this series and the infrequent reports in the literature. At first we suspected that many cases were being missed, but a check of our autopsy files, on more than 5,000 infants and children, yielded only 2 instances.

Personal communication with the medical examiner confirms our impression gained from autopsy review that whatever the incidence, mortality from epidural hemorrhage in children is quite low. The frequency of these cases in our series must indicate that in general, some cases are being allowed to recover spontaneously without evacuation of the clot. Whether permanent damage to the brain occurs in these cases or not, we cannot say.

SUMMARY

1. The anatomy of the calvarium of infants and children is described and illustrated with especial reference to the interrelation of periosteum, skull bones, and dura, and their coparticipation in reactions to trauma.

2. The syndrome of extradural hemorrhage in children is described, based on 20 cases in children younger than 12 years.

3. The treatment of these patients is outlined—18 are living, only 1 with sequelae. Two postoperative deaths are recorded.

CASE REPORTS

CASE 1. Boy, aged 6 years, 7 months, was hit by a stone in the left temple. There was no initial loss of consciousness, the latent period lasting 2½ hours. He was admitted 5 hours after injury, in coma, decerebrate, with respiratory depression. Pulse reported good. Localizing signs were: left pupil dilated more than right, Babinski sign present, and ecchymosis and swelling in left temporal region. At lumbar puncture on admission clear fluid was obtained, pressure, 425 millimeters of water. Complete apnea followed lumbar puncture. Operation was carried out with patient in Drinker respirator. A left subtemporal decompression was done with evacuation of extradural clot and ligation of middle meningeal artery. No fracture was seen. No roentgenogram was made. After operation, spontaneous respiratory rhythm was resumed, but there was no return of consciousness. The patient continued in shock in spite of transfusion. Hyperthermia developed. Death occurred 7½ hours postoperatively. No autopsy was obtained.

This first case in the series was handled 15 years ago, before there was an organized blood bank in this hospital. In light of our present knowledge, lumbar puncture would have been contraindicated since the respiratory center was already depressed and the diagnosis obvious. The facilities of a modern blood bank might have reversed the outcome when one considers how well the patient rallied after operation.

CASE 2. Boy, aged 1 year, 11 months, fell 12 feet to a cement floor. Initial loss of consciousness persisted for 36 hours. A questionable momentary period of lucidity was followed by continuous unconsciousness. Thirty-six hours after injury right hemiplegia developed. Pulse was 80, respirations 28, blood pressure 90/35, temperature 99.6 degrees, cerebrospinal fluid bloody. Roentgenograms revealed a biparietal fracture crossing the superior longitudinal sinus. Supportive therapy was given for 48 hours. Operation was performed 72 hours after injury. The edges of overriding fracture were rongeured away. An extradural clot was evacuated. Decompression was made. Death occurred 16 hours after operation, following circulatory collapse and hyperthermia. Postmortem examination revealed bilateral extradural and subdural hematoma, left cerebral laceration, and longitudinal sinus thrombosis.

This patient, in addition to the extradural hematoma, had serious underlying brain damage which contributed more to his death than the extradural hematoma. However, operation was indicated because of the advancing signs.

CASE 3. Boy, aged 2 years, 1 month, fell from third story window to the soft ground. There was

no immediate loss of consciousness. A latent period of 1½ hours was followed by drowsiness and some vomiting. Localizing signs noted were left parietal cephalhematoma, right hyperreflexia with accompanying Babinski. Temperature was 98.4 degrees, pulse 170, respirations 28, blood pressure 100/45. The fracture line was separated ½ centimeter, extending from the anterior fontanelle on the left downward and posteriorly across the entire extent of the parietal and occipital regions to the foramen magnum. The patient improved with supportive therapy. Subgaleal hematoma continued to increase in size. Operation was performed on the fourth hospital day. The combined subgaleal and extradural hematoma was evacuated through a widely separated fracture line. No specific bleeding point was noted at operation. Patient made an uneventful recovery. He is now leading his class in high school.

This patient did not present the classical picture of extradural hematoma because the widely separated fracture line provided a vent for decompression. Evacuation of the clot was undertaken when patient was in optimum condition, after supportive measures had taken effect and his condition had stabilized.

CASE 4. Boy, aged 2 weeks, had been injured by the application of obstetrical forceps in a breech delivery. The latent period lasted 7 days during which time the patient did well. Then right-sided convulsions occurred. The localizing signs were occipital cephalhematoma, right-sided convulsion. Roentgenogram revealed a depressed comminuted fracture of the occipital bone, left, with extension across the lamboid suture. Lumbar puncture revealed xanthochromic fluid under subnormal pressure containing 1,000,000 red blood cells per cubic millimeter. Operation consisted of débridement of fracture and removal of extradural hematoma, extending from the posterior fossa up over the occipital and parietal lobes on the left. Recovery was uneventful. Patient 10 years later was doing well in school.

This case is atypical. Occipital extradural hematomas are extremely rare. There were no true cerebellar signs. The localizing signs resulted from extension of the hemorrhage up over the cortex. The delay in signs after the injury could probably be accounted for on a basis of the slow accumulation of the clot and self-decompression into the subgaleal space.

CASE 5. Girl, aged 1 year, 9 months, fell two steps, striking right side of head on wood. There was no initial loss of consciousness. A latent period of 15 hours terminated in coma. There were occasional transient bouts of decerebration. Localizing signs were Battle's sign, right, left internal strabismus, left peripheral facial weakness, left spastic hemiplegia. Roentgenogram revealed diastasis at the lambdoid suture; no fracture. Lumbar puncture disclosed clear fluid, 450 millimeters of mercury pressure. Temperature was 101 degrees, pulse 160, respiration 40, blood pressure 110/51. Operation consisted of right subtemporal decompression, partial removal of extradural hematoma via a right subtemporal decompression, and 24 hours later complete evacuation of the extradural hematoma via a bone flap turned around the decompression. The source of bleeding was the tributaries of the lateral sinus. Recovery was uneventful. Patient was very competent in all respects 9 years later.

Operation was carried out in stages because of the weakened condition of the patient. The first operation was delayed 3 to 4 hours awaiting permission to operate.

CASE 6. Girl, aged 8 years, 6 months suffered a lacerated right frontal region by striking her head against a plank while running. There was no initial loss of consciousness. The laceration was sutured by family doctor. Two hours later she developed drowsiness and vomiting which lasted 24 hours, followed by relief from symptoms for 2 days (latent period). Roentgenogram taken 24 hours after the accident showed a compound comminuted depressed fracture of the right frontal bone. Patient was hospitalized elsewhere for 4 days, during which time she vomited, suffered from continuous headache and earache. She was transferred to The Children's Hospital because of onset of disorientation, increased intracranial pressure proved by lumbar puncture and persistent bradycardia 48 to 60. Temperature was 97.6 degrees; blood pressure, 100/40; respirations, 18. Operation was deferred 12 hours in order to hydrate the patient. Then débridement of fracture and removal of large frontal extradural clot was carried out. The operator noted many venous oozing points, which were controlled by endothermy coagulation. The clot was entirely restricted to the frontal space by an intact coronal suture, despite a small dural tear. Recovery was uneventful. Patient was in excellent health 1 year after operation.

We consider this to be a case of extradural hematoma formation resulting from slow venous oozing. The accumulation of the clot was so slow as to simulate a subdural hematoma. It is difficult to explain the exacerbation of symptoms 4 days after trauma without assuming additional hemorrhage or swelling of the clot.

CASE 7. Girl, aged 8 years, 2 months, fell from truck 3 days prior to admission to the hospital. There was questionable loss of consciousness. Transient drowsiness was noted 6 to 8 hours after injury. Patient was up and about the following day; she ate well. Forty-eight hours after injury (latent pe-

riod) drowsiness reappeared accompanied by vomiting, followed by stupor. Seventy-two hours after trauma patient was transferred to the neurosurgical service of The Children's Hospital, at which time she was in deep coma. Localizing signs were swelling beneath the right temporal muscle and bilateral papilledema. Roentgenogram showed a 4 centimeter linear fracture in the right parietal bone. Temperature was 100 degrees; pulse, 70; respiration, 30; blood pressure, 100/60. No lumbar puncture was done. Operation consisted in removal of a large extradural clot via a right subtemporal decompression. Multiple small oozing points were seen and handled with fibrin foam. No large venous channel was open; no arterial bleeding was noted. Patient made an uneventful recovery. She was a competent individual 4 years after operation.

The outstanding feature of this case was the asymptomatic period of 48 hours' duration. No major bleeding points were noted at operation.

CASE 8. A boy, 9 months old, fell out of bed. There was no immediate loss of consciousness. A latent period of 3 hours was terminated by projectile vomiting. Boy was irritable for several more hours and then had a generalized convulsion. Twelve hours later, he was semiconscious. Lumbar puncture revealed grossly bloody spinal fluid. He was transferred to The Children's Hospital the day after injury. His admission temperature was 101.4 degrees; pulse, 110; respirations, 40; blood pressure, 110/58; red blood cells, 2,190,000; hemoglobin 42. The essential physical findings were drowsiness, bulging tense fontanelle; right ipsilateral pupil dilated and fixed; right external strabismus; right facial weakness; left hemiparesis, mild; all reflexes, hypotonic. Roentgenogram revealed no fracture. The sutures showed definite diastasis. Subdural taps on admission were unproductive. Ventricular taps revealed no evidence of subdural hematoma or enlargement of the ventricular system. Lumbar puncture revealed pressure, 300 millimeters of water, 4,000 red blood cells, 100 white blood cells, 94 per cent polymorphonuclear leucocytes. Because of pleocytosis suggestive of a septic process, trephination was not undertaken. Repeated cultures yielded no growth. Tuberculin tests were negative. On the eleventh day after trauma, ventriculography revealed evidence of a mass lesion situated close to the cortex in the right parietal region. Craniotomy was performed and a large extradural clot was exposed and removed. Several points of venous oozing from the dura were controlled with fibrin foam (Fig. 5). The patient made an uneventful hospital recovery. No recent follow-up is obtainable.

Because of the white blood cells in the spinal fluid the traumatic episode in the history was discounted. A neurological lesion resulting from sepsis or thrombosis statistically is more likely than an extradural hematoma in the infant's age group. Therefore, we did not trephine as early in this case as we now would in view of this experience. The pliability of the 9 month old infant's skull and the open suture lines provided accommodation for the mass of the clot.

CASE 9. Girl, aged 6 years, 5 months, fell 3 feet, striking the occiput. She suffered no immediate loss of consciousness. The latent period was terminated 30 minutes later by coma and projectile vomiting. Lumbar puncture revealed clear fluid under normal pressure. Shortly thereafter she returned to consciousness and was considered to be normal. Two days later she became comatose again. This time it was noted that she was developing a left hemiparesis. She was transferred to The Children's Hospital. Upon entry she was drowsy but co-operative. Localizing signs were mild left hemiparesis. Roentgenogram revealed no evidence of fracture. Temperature was 99.8 degrees; pulse, 88; respirations, 24; blood pressure, 106/80. Lumbar puncture revealed pressure to be 150 millimeters of water, clear fluid. Operation was performed immediately after the roentgenogram and 3 days after injury. A right subtemporal decompression with evacuation of extradural clot was carried out. No bleeding point was noted by the operator. Recovery was uneventful. She was a competent individual 2 years later.

This case does not conform to classic standards because of the fluctuation in the state of consciousness, with no fracture. The duration of the lucid interval would suggest a slow source of hemorrhage.

CASE 10. Boy, aged 11 years, fell from a wagon. He was momentarily dazed, then fully recovered. A latent period included mild headache and left frontal hematoma during the first 24 hours and some vomiting. Then, second full recovery. He returned to school 4 days after the accident. Six days after the accident the headache recurred. Fifteen minutes after recurrence of the headache, he fell unconscious to the floor. He entered The Children's Hospital in a mild stupor. Localizing signs were mild hemiparesis, left; dilated fixed pupil, right, (ipsilateral). Roentgenogram revealed a left temporal fracture. Lumbar puncture revealed 1800 red blood cells, normal pressure. Temperature was 97.4 degrees; pulse, 64; respirations 20; blood pressure, 124/70. Immediate operation consisted of right subtemporal decompression with evacuation of an extradural clot, with ligation of main branch of middle meningeal artery, which was the source of bleeding. Recovery was uneventful. No follow-up.

This would be a classic case were it not for the fluctuation in pressure symptoms and the delay before final collapse. Recurrent hemor-

rhage from the middle meningeal artery with intermittent tamponade may explain the discontinuous symptoms.

CASE 11. Girl, aged 1 year, fell 2 feet to floor, striking the occiput. There was no initial loss of consciousness. A latent period was terminated 5 minutes later by drowsiness and vomiting. She was observed overnight on neurosurgical service. She developed localizing signs—cephalhematoma, right posterior parietal region, left hemiparesis, transient dilatation of right (ipsilateral) pupil. Roentgenogram revealed fracture of the right parietal bone, diastasis of the right lambdoid suture. Lumbar puncture revealed clear fluid 252 millimeters of water. Temperature was 97.8 degrees; pulse, 80; respiration, 40; blood pressure, 85/55. Operation was carried out upon appearance of localizing signs and consisted in evacuation of a large extradural clot, ligation of the posterior branches of the middle meningeal artery via a small bone flap. The hemorrhage was entirely restricted to the parietal compartment by the coronal and lambdoid sutures. Normal development two years after operation.

Child was observed each half hour for a 12 hour period. Upon appearance of localizing signs, a diagnosis of extradural hematoma formation was made and operation was carried out. The clot was solid and of at least 100 cubic centimeters in volume. The pliable skull was evidently sufficient to offer accommodation for this clot for some hours in spite of its arterial source. Clinically this patient's condition revealed evidence of unilateral cortical pressure. Burr holes were necessary to distinguish an extradural hemorrhage from edema. We have made many negative burr holes under these same circumstances. Recovery was uneventful. Normal development 2 years after operation.

CASE 12. Girl, aged 1 year, fell 2 feet to the floor, striking the occiput. There was no initial loss of consciousness. Forty-five minutes later she developed drowsiness and vomiting. Patient was admitted to the neurosurgical service, observed every half hour for 12 hours, when she developed localizing signs—small cephalhematoma, right posterior parietal region, left hemiparesis, dilatation of the left (contralateral) pupil. Roentgenogram revealed no line of fracture; diastasis, lambdoid suture, right. Lumbar puncture revealed clear fluid with pressure of 180 millimeters of water; temperature, 96 degrees, pulse, 92; respirations, 28, blood pressure, 114/35. Operation was performed as soon as localizing signs appeared, and was identical with above procedure. Uneventful recovery. Normal development 2 years after operation.

This case is so similar to the last one that no comment is necessary except to suggest that transient dilatation of the pupil contralateral to the clot may have resulted from cortical irritation in the right occipital region (27).

CASE 13. Boy, aged 3 years, 3 months, fell 8 feet to cement. There was no immediate loss of consciousness. Latent period was terminated 1 hour after injury by drowsiness, and vomiting. He became stuporous 19 hours after injury, while in another hospital. He was observed for several hours and transferred to The Children's Hospital. Localizing signs at entry were dilated fixed pupil, left (ipsilateral); right hemiparesis, occasional decerebration. Roentgenogram revealed a small fracture of the left parietal bone and diastasis of the left lambdoid suture. Lumbar puncture revealed clear fluid, with 150 millimeters of water pressure. Pulse was 138, respirations 20, blood pressure 110/80. Immediately after entry preparations were made for operation. Operation identical with that in last 3 cases. Uneventful recovery followed, except for mild hemiparesis, right, and one convulsion. General health was excellent 2 years after operation, with hemiparesis improving.

This boy was obviously failing. In view of the progression of signs, operation was indicated. We are unable to account for the level of spinal fluid pressure.

CASE 14. Boy, aged 7 months, fell 3 feet to the floor. There was no initial loss of consciousness. The latent period terminated 1½ hours later when pallor, drowsiness, and vomiting developed. Two hours later he was admitted to The Children's Hospital in stupor. Localizing signs were Babinski sign, scalp swelling, dilated fixed pupil, right (ipsilateral), hemiparesis, left. No x-ray examination or lumbar puncture were made. Patient was in shock; pulse, 200; respirations, 50; blood pressure, 60/40; temperature, 99 degrees. Immediate preparation for transfusion and operation was made. Operation was identical with that in the last 4 cases except for linear fracture and diastases discovered at operation. Uneventful recovery followed. Normal development for age was noted 1 year later.

The solid clot was approximately 100 cubic centimeters in volume. This constituted a large fraction of the total circulating blood volume of this infant and would therefore account for the state of profound shock.

CASE 15. Boy, 10 years, 11 months, was struck in the left temple by thrown baseball. He was momentarily dazed but there was no immediate loss of consciousness. He walked home with help, a matter of 15 minutes. The latent period was terminated by headache, projectile vomiting, and drowsiness. He

was admitted to The Children's Hospital 1½ hours after injury, in light coma. Temperature was 97 degrees; pulse, 60; respirations, 24; blood pressure, 110/66. Pupils equal, mild right hemiparesis, right Babinski sign. No lumbar puncture was done. No x-ray examination was made. The history and progression of signs were interpreted as sufficient indication for immediate trephining on the left. A large clot, 80 to 90 cubic centimeters, was removed from the posterior parietal region. No fracture was visible. There was a diastasis of the squamosal suture with an ecchymosis in the dura beneath it. Several lacerations in the posterior branches of the middle meningeal artery and veins were clipped, one lacerated tributary to the superior longitudinal sinus was controlled with fibrin foam. Uneventful recovery. Patient was doing well 1 year after operation.

This case has rapid progression of signs. Correlation of the history and ensuing events was sufficient to indicate operation. It is to be noted that a sinus tributary was bleeding in addition to the posterior branches of the middle meningeal arteries and veins.

CASE 16. Boy, 14 months, fell down 12 stairs in a perambulator. He was momentarily unconscious, then recovered. A latent period of roughly 1 hour, was terminated by gradual onset of drowsiness. Two hours after injury, right hemiparesis began. He was received on neurosurgical service 3 hours after injury. He was alternately drowsy and irritable. Swelling in left parietal region was noted, with Battle's sign and suggestion of blood behind the left ear drum. Lumbar puncture revealed clear fluid, pressure 200. Temperature was 98.8 degrees, pulse, 30; respirations, 30; blood pressure 110/80. Patient was observed for 12 hours and given supportive care. Condition remained stable. Roentgenogram revealed left parietal fracture with diastasis of the coronal and lambdoid sutures. Because of localizing signs a trephine opening was made, an extradural hematoma was encountered and removed through a decompression. The source of bleeding was the posterior branch of the middle meningeal artery. Uneventful recovery followed. Normal development was noted 8 months later.

Again the pliable skull of this age group afforded accommodation for the clot which was 4 to 5 centimeters thick, restricted to the parietal compartment.

CASE 17. Boy, aged 12 years, was struck by an automobile. There was doubtful initial loss of consciousness. He entered emergency room a few minutes after accident in full state of consciousness. The latent period ended 1½ hours after injury with the onset of drowsiness, facial weakness, then hemiparesis, and a Babinski reflex. Left (ipsilateral) pupil became larger than right. Roentgenogram revealed a left temporal fracture line crossing the middle meningeal groove. Because of rapidly changing signs and failing circulation within 1½ hours of injury, operation was undertaken immediately. A large clot was evacuated through a left subtemporal decompression. The main branch of the middle meningeal artery was ligated and clipped proximally. Secondary venous bleeding points were either electrocoagulated or treated with fibrin foam. Uneventful recovery followed.

This chain of events was most rapid. It was fortunate that the accident occurred practically outside the gates of a hospital with a well organized neurosurgical service.

CASE 18. Boy, aged 22 months, fell 3 to 4 steps to a tile floor, striking his head. There was no initial loss of consciousness. There was a latent interval of one-half hour after which drowsiness occurred, followed by sleep from which he awakened spontaneously after another half hour. He soon lapsed into a drowsy state again, which progressed to coma in a matter of minutes. He was admitted to the hospital 1½ hours posttrauma. Temperature was 97.6 degrees; pulse, 110; blood pressure, 90/60; respirations, 22. The localizing signs were fixed, dilated right (ipsilateral) pupil; bilateral Babinski; all deep tendon reflexes diminished. Roentgenogram revealed no fracture. No lumbar puncture was done. Immediately prior to operation a decerebrate posture was assumed and respirations became stertorous. Operation was carried out 2 hours after injury, with removal, through a right subtemporal decompression, of a right extradural hematoma which occupied the right parietal space but extended past the lambdoid and squamosal suture lines. The source of hemorrhage was the posterior branch of the middle meningeal artery. No fracture was found at operation but a mobile squamous diastasis was evident. Uneventful recovery.

Clot was restricted by coronal suture anteriorly and occupied the parietal space but extended past the lambdoid suture posteriorly and squamosal suture inferiorly.

CASE 19. Girl, aged 6 years, 6 months, fell from a slide, striking her head on frozen ground. There was no initial loss of consciousness. A latent period of 1 hour was followed by drowsiness. This did not progress to stupor or coma. She was admitted 2 days after injury because of persistent drowsiness and intermittent vomiting. Localizing signs were swelling in the left subtemporal region; no localizing neurological signs. Temperature was 99.6 degrees; pulse, 80; respirations, 20; blood pressure, 115/75. Lumbar puncture revealed acellular fluid under pressure of 230 millimeters of water. Roentgenogram revealed a vertical temporoparietal fracture. Operation consisted of removal of an extensive extradural clot under the frontal, temporal, and parietal bones, through a left subtemporal decompression.

The sources of bleeding were the anterior and posterior branches of the middle meningeal arteries and veins. Good recovery was made.

This case demonstrates that progressive loss of consciousness and blood pressure changes are not necessarily present despite a large intracranial clot.

CASE 20. Boy, 14 months old, fell 2 feet from a bed to a wooden floor. There was no initial loss of consciousness. A latent period of 3½ hours, was terminated by the onset of drowsiness, alternating with irritability and two episodes of projectile vomiting. Drowsiness progressed to stupor by 5 posttraumatic hours. The onset of hemiparesis was suggested by weakness of left side of mouth. Seven hours after fall the boy was admitted to The Children's Hospital in coma and shock. Temperature was 99 degrees; pulse, 160; blood pressure, 110/60; respirations, 24. Left hemiparesis and dilatation of the right (ipsilateral) pupil were noted. Decerebrate patterning soon developed. There was swelling of the scalp over the right lambdoid suture with fracture. No lumbar puncture was performed. At operation a 130 cubic centimeter clot was removed through a combined right subtemporal decompression and bone flap. The source of bleeding was the posterior branch of the middle meningeal artery. Uneventful recovery followed.

The clot was restricted to the parietal and temporal areas by the coronal suture anteriorly and the lateral sinus posteriorly, a factor suggesting that the diastasis of the lambdoid suture permitted it to propagate more posteriorly.

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ACUTE PERFORATIONS OF STOMACH, DUODENUM, AND JEJUNUM

An Analysis of 224 Cases with Late Follow-up Data on 147 Cases of Acute Perforated Peptic Ulcer

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ALTHOUGH many articles have been written on the subject of the perforated peptic ulcer, the majority of these have dealt with the clinical manifestations of the disease and the management of the acute emergency. Relatively few of these reports have contained statistical evidence as to the late follow-up results of those patients who have had emergency, but not definitive, therapy for the disease. For this reason, and because of recent advances in the surgical management of the peptic ulcer, it was thought worth while to review the experience of the Presbyterian Hospital in this problem. It is hoped that with this type of study further light may be thrown on the adequacy or inadequacy of the treatment which we have given these patients in the past.

Perforated peptic ulcers may conveniently be divided into three main groups, with subdivision of the second group into two smaller groups. This classification is a modification of that given by Bockus.

1. Acute perforations. Acute peritonitis is always present in a lesser or greater degree.

2. Subacute perforations. These are usually of pin-point size, they may seal off rapidly, and they are generally of two main types: (a) perforations of the "formes frustes" variety described by Singer and Vaughan in which, although the symptoms of peritonitis are present early in the course of the perforation, they are usually mild and subside rapidly; (b) those perforations which are not associated with the usual symptoms of diffuse peritonitis and pneumoperitoneum. These perforations also may seal off rapidly and are occasionally associated with localized subhepatic gas bubbles (15, 26). If sealing off does not take place small walled-off abscess pockets may develop.

3. Chronic perforation, so-called penetrating ulcers. These include those ulcers which penetrate into neighboring viscera such as pancreas, liver, gall bladder, and transverse colon; or into other structures such as omentum, diaphragm, and anterior abdominal wall.

This review has been restricted to an analysis of only those cases which fit into group 1. In so doing it is quite evident that we have omitted a number of cases in which at some time during the clinical course acute perforations probably had occurred. These cases fall into three ill-defined groups: (1) those cases in which, with rapid sealing off of the perforation, there was rapid clinical improvement and no longer any need for emergency surgical treatment. These relatively few cases could be considered victories for the conservative, nonoperative method of treatment. (In most of these cases actual doubt as to the presence of a true perforation was expressed, and the diagnosis of a perforation was not, as a rule, recorded.) (2) In some of the cases described subphrenic or subhepatic abscesses later developed. Again, these cases were not included in the present study, even though at a later operation, or at autopsy examination, the fact that a perforated ulcer had been present was substantiated. (3) The last group includes those cases in which, during perforation and subsequent sealing off, adjacent viscera had become involved in the inflammatory process resulting in so-cailed penetrating ulcers.

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TABLE I.—ACUTE PERFORATIONS OF STOMACH, DUODENUM, AND JEJUNUM, 1929-1948 INCLUSIVE

		No. cases
Group A	Acute perforation of stomach or duodenum treated by surgical excision or closure	185
Group B	No operation: acute perforation of stomach or duodenum found at autopsy	22
	No operation: no autopsy: typical clinical findings	2
Group C	Miscellaneous acute perforations of stomach, duodenum, and jejunum:	15
	Acute perforation carcinoma of stomach	7
	Acute perforation sarcoma of stomach	3
	Acute perforation sarcoma of jejunum	1
	Acute perforation of gastrojejunal (stomal) ulcer	2
	Acute perforation of jejunal ulcer.	2
	Total	224

The clinical and autopsy records of the Presbyterian Hospital have been reviewed for a 20 year period, 1929 to 1948 inclusive, and a total of 224 cases of acute perforations of stomach, duodenum, and jejunum have been studied. Of these cases, 209 were acute benign perforations of stomach or duodenum due to peptic ulcer (Table I). Only those perforations which were cared for on the ward services were included in this study. A sizable number of private cases was rejected as standardization of follow-up data was desired, and as these patients are not routinely followed in the surgical follow-up clinic.

It is proposed to present certain statistical data in a brief tabular form in order to add to the literature on the subject, and then to discuss in some detail the follow-up results. Those cases in which operation was not performed and in which the diagnosis was established at autopsy are presented briefly in order to develop absolute mortality statistics. The miscellaneous perforations, including those cases due to malignant lesions, are presented very briefly for reasons of general interest.

An exhaustive survey of the literature on this subject has not been carried out; however, pertinent references will be quoted throughout the text.

TABLE II.—AGE AT THE TIME OF PERFORATION

Age, years	No. cases	Age, years	No. cases
15–20	1	51–55	18
21–25	12	56–60	12
26–30	18	61–65	10
31–35	29	66–70	5
36–40	22	71–75	2
41–45	31	76–80	1
46–50	24		

GROUP A

All of the patients in this group were admitted to the surgical service and treated by surgical excision or closure. These cases, 185 in number, form the basis for this study.

Age. The greatest number of perforations occurred during the 4th and 5th decades (Table II and Fig. 1).

Sex. Fifteen of the 185 cases occurred in the female; 8 of these were duodenal, 2 pyloric, 4 were antral in location, and 1 was found in the cardia.

Past history. Past histories of gastrointestinal symptoms with a characteristic ulcer pattern (Table III) were found in 91.9 per cent of all cases. A history of symptoms for a period of less than 1 year was present in 26 patients; for more than 1 year in 144 patients. Fifteen patients had been without symptoms.

When we compare the age of the patients at the time of perforation with the calculated age of the patients at the time they first developed symptoms (Fig. 1) it appears evident that although the perforation may have generally taken place in the thirties and forties, the disease process itself had become established in the twenties and thirties.

Acute exacerbation of the disease. Of the 185 patients, 82 (44 per cent) were recorded as having had an acute exacerbation of the ulcer symptoms of from 1 day to 2 weeks in duration. Fatigue, upper respiratory infections, exposure to cold and damp weather, worry and anxiety seemed to be contributing factors during these periods of acute exacerbation, as also did alcoholism, heavy smoking, and failure to maintain control of the diet.

Precipitating factors in the acute episode. Physical exertion and overdistension of the stomach may have played some part in pre-

TABLE III.—DURATION OF SYMPTOMS PRIOR TO PERFORATION

Duration of symptoms, years	No. cases	Duration of symptoms, years	No. cases
None	15	15–20	6
0–5	85	20–	15
5–10	34	"years"	15
10–15	15		

cipitation of the acute episode in some of these cases. Five of the perforations took place within a few days of having had a gastrointestinal series (of these 5 patients, 4 died of the perforation). Five of the patients volunteered the information that they were straining at stool at the time of the onset. Thirty of the 185 (16 per cent) had been drinking heavily just prior to perforation. A common story in many of these cases was that the patient had consumed perhaps from 6 to 8 beers just prior to the acute onset of the perforation.

Time of day and relationship to meals. The time of onset seemed to bear no statistical relationship to the time of the day in this series, the perforations occurring in a fairly well distributed fashion throughout the 24 hour period. The fewest cases occurred in the early hours of the morning, with only 2 cases occurring at 9 a.m. The largest number of cases occurred in the late afternoon and early evening with peaks at 11 a.m., 7 p.m., and 11 p.m. Although no definite relationships to meals could be found, there remains a distinct impression that the great majority of cases of perforations occurred on a fasting stomach. For example, even though a certain perforation may have taken place at 7 p.m., close analysis of the history of this patient would very probably reveal that the patient had eaten little all day because of nausea and vague epigastric distress, and that little if any supper had actually been eaten.

Seasonal occurrence. The fewest number of cases occurred during the months of April (9 cases) and July (10 cases), and the greatest number during October (26 cases) and January (20 cases). It is also of interest that 110 cases occurred during the six winter months from October to March inclusive, whereas only 75 cases occurred from April to September inclusive. Some of the reports

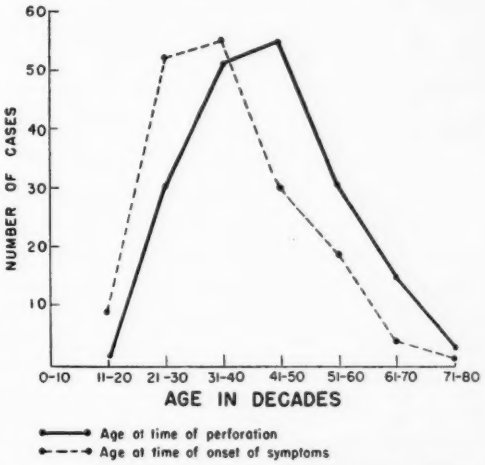

Fig. 1. Comparison of the age of the patient at the time of perforation (185 cases of acute perforation of peptic ulcer of stomach or duodenum) with the age of the patient at the time of onset of peptic ulcer symptoms (155 patients). The exact time of onset of symptoms was not specified in 15 patients, and 15 additional patients had denied having had any symptoms at all prior to perforation.

in the literature on acute perforated ulcer fail to show any seasonal variation in this disease. Other significant reports do show such variation (24). Flood, in reporting on an extensive follow-up survey of 233 medically treated patients from this hospital gave similar seasonal incidences for acute exacerbation of the disease.

Operative technique. With but few exceptions, our patients have been treated by primary closure. It has also been our practice whenever possible to tack down a piece of nearby mesenteric or omental fat in order to reinforce the closure. The technique of closure described by Graham (18) was carried out in many of the cases. Drainage or tamponing of the wound was instituted in 26 cases (14 per cent), the majority of these cases having been treated many years ago. Biopsy of the lesion was carried out, if in the opinion of the operator there was suspicion of neoplastic disease. As regards anesthesia, various agents were used, but no relationship between anesthetic agent and morbidity or mortality could be found in this series.

Time of perforation in relation to surgical treatment. Ninety-one patients (49 per cent)

TABLE IV.—DURATION OF PERFORATION PRIOR TO SURGICAL CLOSURE: RELATIONSHIP TO CULTURE OF PERITONEAL FLUID

Duration in hours of perforation at time of operation	No. of cases	Cultures	
		Positive	Negative
0–3	31	8	16
4–6	60	10	36
7–9	36	16	13
10–12	11	6	3
13–15	10	5	5
16–18	6	3	3
19–21	4	2	1
22–24	7	2	5
25 plus	16	7	5
not known	4		
	185	59	87

were operated upon within 6 hours after perforation. In 47 cases operation was performed in from 7 to 12 hours after perforation and 43 operations were done in cases in which the history of perforation was over 12 hours old. The time of perforation in 4 cases was not known. The relationship between the time of perforation and the culture report of the peritoneal fluid is of interest (Table IV).

Bacteriology of the peritoneal fluid. Cultures were carried out in 146 of the 185 cases. Of these cultures, 59 (40 per cent) were positive and 87 were negative. Streptococcus viridans was the most common organism, having been recovered from 38 cultures. Nonhemolytic streptococci were recovered 15 times, Staphylococcus aureus 12 times, hemolytic streptococci 9 times and Escherichia coli 9 times. A number of other organisms including yeasts and Monilia albicans were recovered in individual cases. Anaerobic organisms were recovered on only 4 occasions.

Location of the perforation. The perforation was found in the anterior or superior walls of the first part of the duodenum in 129 (69.7 per cent) of the cases. The anterior or superior walls of the antrum were perforated in 36 cases (19.5 per cent). There were 13 cases described as "pyloric" in location, and in the other 7 cases the perforations were distributed throughout. As has been pointed out by others, because of the obliteration of anatomical landmarks by edema and inflammatory exudate, the exact localization of the site of perforation at the time of operation is both difficult and inaccurate. Consequently, in this series we have for statistical purposes altered the location of the perforation as recorded in the operative note, if subsequent roentgenograms, operation, or autopsy examination have shown conclusively that the ulcer was located elsewhere. It is partly because of this fact, therefore, that such a high percentage of the perforations in this series have been found to occur in the duodenum. Our figure of almost 70 per cent is similar to that of many of the others found in the literature. The infrequency of perforation of the stomach, with the exception of the antrum, should be emphasized.

Complications. There were 139 complications and 25 deaths (Table V). A gradual decrease in the severity of the complications such as pneumonia, peritonitis, and wound infection has been experienced in the eras corresponding to the institution of the sulfonamides and penicillin, even though the frequency of such complications has remained high. Paralleling this decrease in the severity of complications, there has been a marked decrease in the operative mortality.

Major pulmonary complications, such as massive atelectasis and pneumonia, occurred in 41 different cases and in 4 of these patients were followed by empyema. Pleural effusions were occasionally noted but were not included in the tabulation. The diagnosis of generalized peritonitis was made 13 times and peritoneal abscesses occurred in 12 different patients. There were 20 wound infections and 16 wound disruptions. Major pyloric obstruction was encountered 9 times and in 8 cases massive bleeding was exhibited in the immediate postoperative period. The diagnosis of thrombophlebitis was infrequently made in the patients of this series, and only 3, nonfatal, cases of pulmonary embolism were recorded. A fourth patient, who had had postoperative pneumonia with bilateral pleural effusion, died suddenly on the 50th postoperative day. No autopsy was performed,

TABLE V.—POSTOPERATIVE DEATHS: RELATIONSHIP TO AGE OF PATIENT, DURATION OF PERFORATION PRIOR TO OPERATION, AND CULTURE OF PERITONEAL FLUID

Postop. day	No. of deaths	Chief causes of deaths	Age, years	Culture	Hours of perforation prior to operation
1	4	Peritonitis (4)	29, 42, 61, 72	+ (3) not done (1)	20, 23, 24, 36
2	2	Cerebral thrombosis (1) Peritonitis (1)	44, 67	+, +	8, 9½
3	4	Pneumonia and peritonitis (4)	33, 39, 45, 48	+, —, —, —	24, 24, 48, 48
4	3	Pneumonia and peritonitis (1) Pneumonia, peritonitis, and delirium tremens (1) Pneumonia (1)	41, 53, 54	+, +, —	4, 7½, 36
7	3	Pneumonia (2) Massive hemorrhage (1)	27, 54, 67	+, —, —	2½, 16, 96
8	2	Peritonitis (1) Pneumonia, empyema, and peritonitis (1)	50, 70	+, +	5, 72
13	1	Cardiac arrest at operation with subsequent decerebrate rigidity	41	+	5½
14	1	Massive hemorrhage	59	—	2½
17	1	Perforation of 2 acute gastric ulcers with peritonitis	50	+	5
36	1	Massive hemorrhage	46	not done	72
41	1	Massive hemorrhage	63	—	1½
50	1	Pneumonia, pleural effusion. Sudden death ? pulmonary embolism	51	+	3
90	1	Multiple peritoneal abscesses pneumonia, empyema	29	—	60

but it is believed likely that he had had a massive pulmonary embolism.

Three complications are of interest. There were two fistulas; one, a gastric fistula, which closed spontaneously on the 11th postoperative day and the other, a duodenal fistula, which closed spontaneously on the 20th postoperative day. The third complication was the perforation of 2 acute gastric ulcers in a 50 year old man, 17 days after repair of a perforated anterior wall duodenal ulcer, resulting in peritonitis and death. At autopsy, "kissing" duodenal ulcers were found and multiple acute gastric ulcers were seen as well as the two large perforations mentioned. The right gastric artery was found to be thrombosed. Prior to death, the patient had developed bronchopneumonia and a partial wound disruption.

Postoperative deaths. There were 25 deaths (Table V) giving a combined operative mortality of 13.5 per cent. For the last 4 years of this study the operative mortality was 3.3 per cent (Table IX). Of this group of 25, 8 were between the ages of 41 and 50 years, 6 were younger than this, and 11 were older. Of the deaths, 11 occurred in patients in whom the perforation had been less than 12 hours old. In 3 patients, the perforation was between 12 and 24 hours old; in 11 patients, the perforation was more than 24 hours old. Cultures were positive in 14, negative in 9, and not done in 2 cases. Four of the deaths occurred following a barium meal and 4 occurred in patients who had been drinking at the time of perforation. Only 1 of these patients had been known to have had a meal just prior to perforation. With the exception of those cases listed, the majority of the perforations seemed to have occurred on an empty stomach.

Follow-up studies. These 185 cases represent 179 different patients; perforation recurred in 6 cases and repair was carried out a second time. Of the 179 patients, 150 were followed at frequent intervals in the Vanderbilt Clinic. Of these, 143 patients are suitable for an analysis of postoperative results (Table VI). This excludes those who died following perforation (25 patients), those in whose cases no follow-up data were obtained (4 patients), those who had prophylactic gastrectomy in the immediate postoperative period (6 patients), and 1 patient in whose case gastrec-

TABLE VI.—POSTOPERATIVE SYMPTOMS IN 143 PATIENTS WITH SIMPLE CLOSURE OF PERFORATED PEPTIC ULCER

Years of follow-up	Total No. patients	Patients with major symptoms at any time	Per cent of total	Patients with mild symptoms at any time	Per cent of total	Patients with no symptoms	Per cent of total
0– 1	20	13	65	0	0	7	35
1– 3	21	16	76	4	19	1	5
3– 5	29	19	66	7	24	3	10
5–10	45	36	80	2	4	7	16
10–20	28	24	86	1	3	3	11
	143	108	75.5	14	9.8	21	14.7

tomy was performed at the time of perforation. Two of the patients in whom perforation had recurred during the follow-up period had also received prophylactic definitive surgery; in one case a gastrectomy, and in the other, a gastroenterostomy. A gastroenterostomy had been performed in only one other patient with perforated ulcer, and this patient had died following the operation. In all, 50 patients were lost to the follow-up clinic throughout this 20 year period. Of these 50, 15, when last heard from were having symptoms of peptic ulcer. Eighteen other patients of the group of 143 died during the 20 year period of follow-up. Two patients died following a second perforation; 1 died of a massive hemorrhage from the peptic ulcer, 4 died of postoperative complications in this and other hospitals, 2 died of unknown causes, and 9 died of intercurrent disease. Seven deaths, therefore, can be attributed to peptic ulcer, 4.9 per cent of the cases which have been followed.

Of the 143 patients followed, 108 continued to have recurring symptoms characteristic of a peptic ulcer. Fourteen patient experienced occasional mild symptoms and mild exacerbations requiring medical control, attention to diet, and occasional clinic visits. Twenty-one of the patients followed have had no symptoms at all except perhaps for occasional belching and heart-burn.

We may state, therefore, that peptic ulcer symptoms were experienced postoperatively in 122 of 143 patients, or in 85.3 per cent. Severe symptoms were experienced by 108 or 75.5 per cent.

Operative procedures in the follow-up period. Fifty-five (38.5 per cent) of those patients followed required a total of 56 subsequent definitive operative procedures. Partial gastrectomy was carried out 41 times and gastrojejunostomy 7 times. Six of the patients required closure of a reperforation. A transthoracic bilateral vagotomy was carried out on one occasion and an excision of a bleeding ulcer with gastrorrhaphy was carried out once.

Symptoms in the follow-up period. The major postoperative symptoms in the 147 cases (143 patients) have been compared with the major preoperative symptoms experienced prior to perforation in all 185 cases. Two of the patients who had second perforations in the follow-up period are not included in this table because definitive surgery was performed in each case soon after the second perforation. Postperforation symptoms in the other 4 cases have been included. Not all of the patients who had major peptic ulcer symptoms (viz.: pain, bleeding, obstruction, or perforation) in the preperforation period had major peptic ulcer symptoms in the period of follow-up and vice versa. The statistics on these patients are therefore combined in order to develop a more true incidence for each of these symptoms during the life history of each ulcer case, as observed in this follow-up period. The major peptic ulcer symptoms for each period have been listed in Table VII.

Pain (ulcer type). Of the 15 patients who denied any history of gastrointestinal distress prior to perforation, 3 died in the immediate postoperative period and 2 were subjected to prophylactic gastrectomy. Three experienced typical ulcer pain in the follow-up period and 2 others had mild symptoms easily controlled

TABLE VII.—MAJOR PEPTIC ULCER SYMPTOMS*

Type of symptoms	Major preperforation symptoms (185 cases, 179 patients)	Per cent of total cases	Major postperforation symptoms (147 cases, 143 patients)	Per cent of total cases
Pain (ulcer type)	170	91.9	100	68.0
Bleeding (hematemesis and/or melena)	39	21.1	28	19.0
Obstructive symptoms (pyloric obstruction, pylorospasm)	34	18.4	37	25.2
Previous perforations	8 (7 patients)	4.3	Reperforations 9 (9 patients)	6.1
Total cases with symptoms	170	91.9	110	74.8

*The values in this table cannot be compared with those of Table VI as here we have added to the total number of major symptoms experienced, the preperforation and postperforation symptoms of the 9 cases of reperforation in the follow-up period (only 4 were resubjected to follow-up studies).

by diet. In 1 of these perforation occurred a second time 6½ years later, even though the patient had been relatively free of symptoms during this period. The other 5 were followed 2 months, 6 months, and 9½, 10, 15½, and 15 years before becoming lost to the follow-up clinic.

Bleeding. Sixty-seven cases of bleeding (representing 62 patients) occurred both before and after perforation, clinical bleeding, therefore, occurred in 62 of the 179 patients (34.6 per cent). These figures, do not include the cases of bleeding at the time of perforation (5 cases) or those cases of bleeding in the immediate postoperative period (12 cases). No deaths occurred from hemorrhage taking place at the time of perforation. Of the 12 patients who experienced hemorrhage in the immediate postoperative period, 4 were subjected to gastrectomy and survived, 2 others were subjected to gastroenterostomy, and 1 of these patients died. Four other patients who were treated medically died. In this group there were, therefore, 2 survivals following medical therapy. In the group of 28 cases of bleeding during the follow-up period, death from massive hemorrhage occurred in 1 patient. Eleven other patients with severe bleeding were subjected to gastrectomy with survival. The 16 remaining patients received only medical therapy. Bleeding was a sufficiently severe symptom, therefore, to require gastrectomy in 15 patients and gastroenterostomy in 2. Six deaths (3.3 per cent of 179 patients) can be attributed to massive hemorrhage.

Obstruction. Pyloric obstruction was a major symptom on at least 1 occasion in 66 of 179 patients (36.8 per cent). Minor degrees of pylorospasm or actual obstruction which responded to medical therapy were even more common. Because of the difficulty in accurate assessment of this condition from the records available, no further statistics will be presented.

Repeated perforations. In the 143 patients subjected to follow-up studies there were 4 cases of acute reperforation treated by surgical closure, accounting, therefore, for the total of 147 cases. (A fifth patient had a prophylactic gastrectomy soon after closure of the perforation, and a sixth patient was subjected to a gastrojejunostomy at the time of closure.) In 3 other cases perforation occurred and the patient died without operation. In a tenth case perforation was found to have recurred and a localized abscess was found during the course of gastrectomy; this case, however, is not included in these statistics. The percentage of reperforation, therefore, in the patients followed, is 9 ÷ 143, or 6.3 per cent. In 16 of the total number of 179 patients included in group A, perforation occurred on more than 1 occasion; 1 of these patients had 2 previous perforations.

GROUP B

Patients who were not operated on and who died of the perforation. There were 24 cases in all (Table VIII).

Two of these were not confirmed by autopsy examination, but in each case free air was found under the diaphragm on x-ray examination. One case was in a 65 year old male with a 12 year history of symptoms, including repeated hospital admissions for gastric hemor-

TABLE VIII.—NO OPERATION: ACUTE PERFORATION OF STOMACH OR DUODENUM FOUND AT AUTOPSY

	No. Cases
A. Typical ulcer history (no associated major pathology of etiological significance)	8
B. No history, admitted in extremis (no associated major pathology)	2
C. Good ulcer history, but associated with major pathology of possible etiological significance..	
Following cholecystectomy and gastrotomy..	1
Following cholecystostomy for carcinoma of hepatic duct	1
Following liver biopsy; associated carcinoma of esophagus	1
Carcinoma of lung (no operation)	2
D. No history of gastrointestinal symptoms	
Sepsis	2
Phosphorus poisoning	1
Hydrocephalus (10 mos. old)	1
Fractured hip, open reduction, pneumonia	1
Following prostatectomy	1
Periarteritis nodosa	2
Acute rheumatic fever	1
	24

rhage. The other case was in a 10 month old female infant with congenital internal hydrocephalus. Cauterization of the choroid plexus had been carried out on 3 separate occasions. She had finally begun to have hematemesis as well as melena, and when she died, free air under the diaphragm was established by x-ray examination. Of the 24 perforations, 16 took place while under observation in the hospital. In 14 of the 24 there was associated bleeding. Five patients exhibited, and probably died directly because of, massive hemorrhage rather than because of peritonitis. Three of the patients had previous perforations repaired at the Presbyterian Hospital. Thirteen of the group gave clear histories of gastrointestinal symptoms. Two of the patients were admitted in coma and adequate histories were not obtained. Two cases are of interest because of widespread periarteritis nodosa. One of these was in a 65 year old man; the other in a 13 year old boy. Both were under observation on the medical service. The condition of each had gradually deteriorated, being characterized by fever, petechial hemorrhages, anorexia, and gastrointestinal symptoms, including hematemesis and melena. At autopsy numerous generalized vascular lesions were found in each case including the gastrointestinal tract and the regions of each perforation. Numerous ulcerations throughout the gastrointestinal tract were found in one, whereas in the other, the lesions were limited to the duodenum. The perforation was in the anterior wall of the first part of the duodenum in one, and in the anterior wall of the antrum in the other.

Multiple perforations. If we add together both the number of cases of perforated ulcer operated upon (group A) and those of acute perforations found at autopsy (group B) we have a total of 209 cases representing 200 patients (9 of the patients with 2 perforations and admission to this hospital on each occasion; 7 others with previous perforations repaired in other hospitals, 1 of these with perforations on 2 previous occasions). In these patients, then, we have a total of 17 repeat perforations, or an incidence of 8.5 per cent. Some of the acute perforations which were found at autopsy and which had occurred during the course of other diseases should probably not be included in this calculation as they do not actually represent true peptic ulcers. If this change were made, the incidence for reperforation would be approximately 9 per cent. It is also interesting to note that 3 of the 21 patients who did show a satisfactory postoperative course, in the period of follow-up had previous perforations.

In the collected cases reported by DeBakey in 1940, he found that reperforation had only taken place in 74 of 6,538 cases, an incidence of 1.1 per cent. Other incidences reported are those of Ulfelder and Allen (44), 2.7 per cent of 334 cases; Cohn, 4 per cent of 300 cases; Moore and Hendricks, 5 per cent of 101 cases; Shallenberger and associates, 6 per cent of 50 cases; and Estes and Bennett, 12.7 per cent of 63 cases. The incidence of 8.5 per cent reported in this paper seems quite high in view of the careful postoperative care and follow-up generally administered to these patients.

Of these 209 perforations, 32 occurred while the patient was under observation in the hospital. Two others occurred while visiting the out-patient department. Fifteen of these 34 patients died.

Absolute mortality statistics. The mortality of benign gastroduodenal perforations has decreased gradually through the years con-

TABLE IX.—THE POSTOPERATIVE AND ABSOLUTE MORTALITY IN 185 CASES OF ACUTE PERFORATED PEPTIC ULCER

Year	No. cases	No. deaths postop.	Per cent operative mortality	No. deaths, no operation (Table VIII)	Total cases	Total deaths	Per cent absolute mortality
1929–33	29	9	31.0	3	32	12	37.5
1934–38	49	10	20.4	9	58	19	32.8
1939–43	47	4	8.5	6	53	10	18.8
1944–48	60	2	3.3	6	66	8	12.1
	185	25	13.5	24	209* (208)	49	23.6

*As the 209th case is one in which patient died of perforated acute gastric ulcer 17 days after suture repair of a perforated duodenal ulcer, it is not included in the absolute mortality rate to avoid duplication.

currently with improvements in surgical technique and improvement in the management of these patients. Marked divergence in mortality statistics are noted throughout the literature for any one period depending on varying methods of statistical analysis, as well as on the skill of the individual surgeons and on the varying methods of treatment used in the different clinics.

Moynihan, who was one of the first to present a significant series of these cases, had an operative mortality of 33.3 per cent in a series of 27 cases reported in 1908 (31). Twenty years later, in a collected series of 237 cases from the Leeds General Infirmary, he reported an operative mortality of 23.1 per cent for 211 cases of perforated duodenal ulcer, and 26.9 per cent for 26 cases of perforated gastric ulcer (32).

DeBakey, in a comprehensive review of this subject, found that in a collected series of 15,340 patients operated upon between 1930 and 1940, there was a combined operative mortality of 23.4 per cent. More recent statistics show a variation of between 6 and 18 per cent (19, 14, 28, 25, 30, 27), and there is evidence that in the past few years, due in a large part to the advent of antibiotics and chemotherapy, the mortality now ranges between 1 and 5 per cent (27, 4, 11). These, of course, represent selected cases: i.e., those of operation. The absolute mortality for this disease is still high (Table IX).

GROUP C

Miscellaneous Perforations

Carcinoma of stomach. There were 7 acute perforations associated with acute diffuse peritonitis. Of these, 6 were in the anterior wall of the stomach and 1 communicated with the lesser sac through a perforation of the posterior wall. Closure of the perforation was carried out in 2 patients followed by a subsequent gastrectomy in each case. The perforations in the other 5 patients were found at postmortem examination.

It is of interest to note at this point, that none of the 143 patients followed in this series developed carcinoma of the stomach during the course of the study. Flood similarly noted that none of his 233 medically treated cases followed for up to 20 years developed cancer of the stomach.

Lymphosarcoma. There were 3 cases (representing 2 patients) of perforated lymphosarcoma of the stomach, resulting in generalized peritonitis. In each case the growth perforated through the anterior wall of the pyloric antrum. One patient died without having come to operation. The other case is of considerable interest. The patient was a 19 year old boy who had repeated epileptiform attacks throughout childhood. Two months prior to admission, he began to have vague epigastric distress, tarry stools, and weight loss. Three hours after taking barium for a gastrointestinal series, perforation through the anterior wall of the pyloric antrum took place. Closure was carried out in the usual manner and biopsy of the stomach and of an enlarged superior gastric gland was made. The histological diagnosis was that of lymphosarcoma, reticular cell type, with metastases to superior gastric glands. A little over 3 months later, a reperforation took place which was close to, if not in the same, area of the antrum. Closure

and biopsy were again carried out. Many adhesions were present but there were no evidences of metastases. Deep x-ray therapy was given before this second operation and afterward. The microscopic slides were reviewed once again, and the diagnosis was confirmed. This patient has been followed for 17 years and at last report (January 11, 1949) was alive and well.

Stomal ulcers. There were 2 stomal ulcers with acute perforation and associated generalized peritonitis. In one case the perforation was marginal and included both stomach and jejunum. In the other case, the perforation was jejunal and was located directly opposite the stomal opening.

An exhaustive search through the records of all the peptic ulcers would, perhaps, have uncovered a few additional cases.

Jejunal perforations. There were 3 acute perforations distal to the ligament of Treitz in patients who did not have gastroenterostomies. One case was secondary to a lymphosarcoma of the jejunum; the second case was in a patient with advanced thromboangiitis obliterans; and the third case was in a patient who was being treated for polycythemia vera and who had reportedly perforated a peptic (gastroduodenal) ulcer several years prior to his emergency operation in this hospital.

DISCUSSION

Many years ago it was a commonly held belief that once an ulcer had perforated and healing had taken place, the patient would in many cases be cured of the disease. Therapy in those days consisted of simple closure, excision, or infolding of the ulcer, either alone or combined with a gastroenterostomy as originally advocated by Moynihan (31, 32), if danger of obstruction existed. This theory was expressed in many of the older textbooks and it formed the basis for the practice of cauterization of peptic ulcers as advocated by Balfour in 1918. Of the fact that many of these ulcers may heal subsequent to perforation, we now have no doubt. Similarly, it is still true that a few of these patients may recover completely and, owing to the fact, most probably, that they realize the error of their ways, never again manifest peptic ulcer symptoms. However, we now feel that failure of some of these observers of years gone by to become aware of the high recurrence rate in these patients was due largely to inadequacy in the length of their follow-up studies. Knowledge as to the true nature of peptic ulcer has been gradually unearthed through the years. Although the etiology of the disease in all of its many facets has not been completely revealed, we now speak of the "ulcer diathesis"; we are now aware of its characteristic periodicity, chronicity, and in some cases its intractability, and finally, some observers have even gone so far as to call it incurable (2).

The protean nature of peptic ulcer is now well recognized. It has been called one of the wound stripes of modern civilization, and the increasing frequency of the disease was recognized and commented upon by Moynihan and others at the turn of the century. An estimated 5 to 12 per cent of the population are afflicted with peptic ulcers at some time during the course of their lifetime (23), and autopsy statistics show that from 5 to 6 per cent of all persons have peptic ulcers at the time of death (22, 34).

That most of these patients remain free from symptoms of ulcer activity, most of the time, we well know, and that the majority of these patients are content to remain under medical management despite recurrent distress has been recently emphasized (16). Where, then, does the patient with perforated peptic ulcer fit into the scheme of the present day management of this disease? In answering this hypothetical question, knowledge as to the follow-up statistics in these patients is of the utmost importance.

Thompson in 1939 obtained follow-up reports by questionnaire from 51 patients of a total of some 500 cases of perforated peptic ulcer. Of these patients, 61.2 per cent replied that they had continued to have peptic ulcer symptoms; 66 per cent of these patients had been followed for longer than 5 years. In the more recent literature, we find varying recurrence rates of 56 per cent (39), 67 per cent (33), 68 per cent (25), 69 per cent in cases of duodenal ulcer and 66 per cent in cases of

gastric ulcer (30), 82.5 per cent (21), and 94.4 per cent (14). This variation in follow-up data as to the recurrence rate is partly due to an individual interpretation as to the severity and significance of various gastrointestinal complaints, and similarly a difference in criteria as to just what constitutes a recurrence of the disease.

The variable statistics are also in part due to the small numerical size of some of the groups which have been followed, and the relatively small number of years which some of the follow-up statistics represent.

That the length of follow-up is of the utmost importance in the interpretation of these data is emphasized in Table VI. Kingsbury and Schilling made a note of this fact when they showed that whereas only 42 per cent of patients had recurring symptoms by the end of the first postoperative year, 68 per cent of those followed more than 1 year had symptoms. St. John and Flood (36) and Flood (16) have shown similar statistics in the follow-up of patients with duodenal ulcer who have had at least one medical hospital admission for either severe pain, bleeding, or obstruction. (Those patients first admitted to the hospital with perforated peptic ulcers were excluded from this study.) Whereas 65 per cent of these patients had recurrent symptoms by the end of 2 years, only 48 of 233 patients (21 per cent) had remained continuously free of symptoms with an average follow-up of 5.9 years. These patients had been followed in the Vanderbilt Clinic and had been under reasonably strict medical control. To quote Flood, "In the succeeding years the number of patients remaining entirely free from symptoms grows progressively smaller, and after 10 or 15 years only a small proportion of the original group have remained symptom-free. Thus it was only the exceptional patient who did not have a recurrence if followed for a sufficient length of time."

In this series of 233 patients, 30 (13 per cent) required definitive surgery. Three required operation because of severe bleeding and 10 required operation because of persistent pyloric obstruction. In 7 cases persistent pain was given as the main reason for surgery, and in 10 cases operation was carried out because of frequent recurrences. Only 2 of the ulcers perforated during the course of the study. Five of these 233 patients died of causes related to ulcer, giving a mortality of 2.1 per cent.

These statistics have been quoted as it is very useful to compare the patient with perforated peptic ulcer and the patient admitted to the medical ward. It is immediately apparent, for example, that the patient with perforated ulcer represents a much more intractable form of the disease. The absolute mortality of 12.1 per cent for perforated peptic ulcers for the years 1944 to 1948 is to be compared with the medical mortality of 2.1 per cent, which includes perforation as well as massive hemorrhage and other causes of death. The percentage of surgical procedures required in the follow-up period of the perforated ulcer patient, 38.5 per cent, can be compared with the 13 per cent requiring surgery in the medically treated group. The incidence of perforation during the course of the follow-up study, 9 of 143 patients (6.3 per cent) can be compared with the incidence of perforation in the medically treated group, 2 in 233 patients (0.86 per cent). Finally, whereas 21 per cent of the medical ulcer group remained symptom-free, only 15 per cent (21 of 143 patients) of the perforated ulcer group remained symptom-free. It should be pointed out that the follow-up periods for these two groups of patients have been relatively the same.

It might be said that the management of the patient with perforated ulcer has passed through two stages and is now entering on the third stage. (1) The tendency in former years was to treat the patient with perforated ulcer medically throughout the follow-up period. To a certain extent this treatment was casual, perhaps even negligent in some cases, because of the widespread belief that perforated peptic ulcers are different, and that many of them will be cured. (2) In more recent years, with the growth of the concept of the ulcer diathesis, it has become increasingly obvious that the patient with perforated ulcer should at least be treated as the patient with any other peptic ulcer. That is, he should receive expectant follow-up therapy,

and complications should be taken care of as they arise. (3) It is now the belief of some surgeons that the patient with an ulcer which perforates has thereby shown evidence of the intractability of the disease, and should, therefore, be subjected to prophylactic elective gastrectomy, usually within 3 to 4 weeks after recovery from the acute episode. The statistics presented in this paper would tend to support those surgeons who carry out this practice. Furthermore, the present day attitude of the lay public also serves to support this trend. Whereas in former years the majority of ulcer patients were content to remain under medical management, nowadays because of improved surgical methods and because of a significantly lowered operative mortality, increasing numbers of patients are willing to have, and even desire, surgical therapy. This desire on the part of the public also speaks well for the success which modern day surgical therapy is attaining in the prevention of postoperative morbidity as well as in the prevention of recurrences of the disease.

Present day operative mortality for subtotal gastrectomy has for some years been in the neighborhood of 1 to 5 per cent in the hands of most capable surgeons (1, 5, 17, 29, 35, 37, 41, 46, 48). Many of these statistics include all varieties of complicated cases such as secondary resections in case of stomach ulcer and gastrojejunal colic fistulas and ulcers penetrating into the pancreas and liver. There is now ample evidence to show that the operative mortality in elective gastrectomies performed on simple uncomplicated ulcer patients, such as would be the case in most post-perforated ulcers, is well under 1 per cent. Prophylactic gastrectomy would, therefore, seem to be the treatment of choice in all cases of perforated peptic ulcer.

In order to emphasize further the dangers involved in not carrying out prophylactic gastrectomy in these cases of intractable ulcer, certain features of the ulcer diathesis as they pertain to the management of the perforated ulcer patient are here summarized. These are: (1) the large size of some ulcers. In 1 of our cases perforation took place in an ulcer which measured 6 by 3 centimeters. In another case, the ulceration completely encircled the stomach near the cardiac orifice. Large ulcers of this type are rarely seen in the duodenum, but they may also be seen at the level of the incisura angularis where, occasionally, they may give rise to the well known hourglass contracture. (2) The danger of hemorrhage in association with perforation, especially if the ulcer is a large one, should be kept in mind. This applies particularly to gastric ulcers at the lesser curvature and posterior ulcers where there is associated penetration of the pancreas. In the duodenum, ulcers on the superior and posterior walls are most to be feared because of the proximity of the gastroduodenal and pancreaticoduodenal arteries. (3) The not infrequent occurrence of multiple ulcerations and erosions, acute or chronic, gastric or duodenal should be stressed. Although the characteristic peptic ulcer is single, circular and "punched out," multiple ulcers occur in a high percentage of cases. (4) In this regard, it is well to keep in mind that one of these other ulcers (which may be histologically either acute or chronic) may perforate or may bleed at any time during the postoperative course. The futility of attempting to cure the disease through local excision of a bleeding or perforated ulcer (when multiple ulcerations exist) rather than carrying out a formal gastric resection is readily apparent. (5) The extreme indolence and slowness to heal of some of these ulcers make it mandatory to plan post-operative care (nasogastric suction, feeding, etc.) accordingly. (6) The danger of using absorbable suture material was brought to our attention in several of our cases in which it was found that early dissolution of the suture material had permitted the perforation to reopen. (In 1 recent case, not included in the series, this factor was an important one in leading to the death of the patient.) The advisability of always covering the sutured perforation with mesenteric fat or omentum is well recognized. (8) Finally, it is well to emphasize the intractability of, and the tendency to, recurrent perforation in these cases even though, as in one of our cases, the patient had been under medical control for 8 years and had had relative freedom from ulcer symptoms for most of this period.

The treatment of the perforated peptic ulcer. Simple closure of the perforation is still the preferred method of treatment of most clinics in this country; for the surgeon's main responsibility is to save life. It is proposed, however, that prophylactic surgery be strongly considered in the immediate postoperative period of these patients, barring the future development of an adequate form of medical therapy.

Two extremes in the operative treatment of perforated ulcers have been advocated in recent years, and should be briefly described. The first of these is the primary gastrectomy for perforated ulcer, and the second is the conservative, or nonoperative, method of treatment. We have had experience with a number of primary gastrectomies in the past 2 years, all with signal success. (These cases have not been included in the present study.) We have also had some experience with the conservative method of treatment. Primary gastrectomy is a procedure which is being carried out in increasing numbers of selected cases in various clinics. Following von Haberer's success with this procedure in 1919, it was adopted as the procedure of choice in selected cases by many European surgeons, with the exception of many of those in Britain and Scandinavia where conservatism held sway, as it had in this country. Remarkably low mortality figures were obtained with this procedure even before the onset of the present day antibiotic era. That even lower mortality figures are attained today is evident from the statistics given by Bobbio and others. Yudin (13) had been one of the most ardent and most successful advocates of this method. Graves, Strauss, and Bisgard are among those who have written on the subject in the American literature.

At the other extreme, conservative nonoperative treatment has its present day advocates, and unusual success has been attained with its proper usage. Originally advocated by Wangensteen in 1935 (47) for the management of: (1) the doubtful case, (2) the localized perforation (formes frustes type) admitted to the hospital late with evidence of having sealed off, (3) the very late case with no evidence of continued leaking, and (4) the poor risk patient, the treatment was then resurrected and applied in recent years to the treatment of the acutely perforated ulcer by Bedford-Turner in 1945. Visick, Bingham, and Seeley and associates have also applied this method to the treatment of the acutely perforated ulcer. The essentials of this treatment consist of the constant use of the indwelling nasogastric tube, the administration of nothing by mouth, the use of sedation and antibiotics. There has been striking success with this method but it is generally agreed that surgery, if available, is still the preferred method of treatment.

SUMMARY

In this study 224 perforations of the stomach, duodenum, and jejunum have been summarized, with special stress being laid on 185 cases of perforated peptic ulcer which were treated surgically. In 91.9 per cent of the 185 cases past histories of gastrointestinal symptoms characteristic of peptic ulcer were given.

The precipitating factors of the acute episode, the season, the time of day, the location of the ulcer, bacterial spectrum of peritoneal fluid, postoperative complications, and deaths have all been briefly described.

Of the 185 cases, 147 were followed in the Vanderbilt Clinic for intervals up to 20 years (52 per cent of the patients were followed for more than 5 years), 85.3 per cent of all patients followed continued to have symptoms of peptic ulcer. The symptoms were severe in 75.5 per cent of the cases, and 38.5 per cent of the patients required additional surgery. Bleeding, as evidenced by hematemesis and melena, occurred in 19 per cent of the patients during the follow-up period. Taking the past history into account, 34.6 per cent of the total number of patients gave a history of bleeding on at least 1 occasion. Obstructive symptoms were experienced on at least 1 occasion in 36.7 per cent of the patients. The incidence for reperforation in the total number of 209 was 8.5 per cent. Reperforation in those followed took place in 6.3 per cent of cases. Massive fatal hemorrhage took place in 11 of the 209 cases, or 5.3 per cent. In 5 of these patients massive fatal hemorrhage occurred at the time of perforation.

Of the total of 209 operative and non-operative cases of perforation, 34 occurred while the patient was under observation in the hospital; of these, 15 patients died. The absolute mortality for all cases of perforated ulcer through this 20 year period was 23.6 per cent. The operative mortality was 13.5 per cent; during the last 4 years of the study, this fell to 3.3 per cent.

CONCLUSIONS

Perforation of a peptic ulcer of stomach or duodenum is proof of the intractability of the ulcer diathesis in that particular patient. It has been pointed out in this paper that the recurrence rate of peptic ulcer is high (85.3 per cent) and that in a high proportion of these patients the symptoms are severe. It is also pointed out that even in the absence of recurrent symptoms the danger of reperforation is present. It is further emphasized that the danger of massive hemorrhage and of reperforation exists even in the immediate postoperative period of these patients. In the immediate postoperative period prophylactic surgical therapy (perferably subtotal gastrectomy) is advised for all patients with perforated ulcer. Primary gastrectomy may be indicated in a selected number of these patients.

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THE POSTOPERATIVE USE OF ADRENAL CORTICAL EXTRACT

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PATIENTS undergoing major surgery during periods of intense heat waves, particularly in certain areas of this country such as the Southwest, are subjected to an additional hazard. During periods of extreme heat, the postoperative course is frequently complicated by the rapid onset of a severe febrile reaction, either during the course of surgery or postoperatively, which may persist several days. The patients are in critical condition, without there being any clinical explanation other than heat stress, and are not signally benefited by the usual therapeutic measures. Patients occupying hospital rooms which are not air-conditioned appear to experience the reaction most frequently. Occasionally, placing circulating air over large quantities (100 pounds or more) of ice in the room has been resorted to in an effort to combat the severity of the reaction, which in certain respects simulates heat stroke and has been attributed to intense heat.

The two noxious agents, heat and the trauma of the surgical procedure, undoubtedly act as intensely exciting stimuli to the adrenal cortex, and certain changes in these patients appear to be related to altered adrenal activity. The response of the organism to stressful (alarming) stimuli has been comprehensively investigated by Selye and his coworkers (35–38). The concept of the general alarm reaction as an expression of pituitary-adrenal secretory activity has assumed great significance, in that the phenomenon is encountered and must be considered in practically all fields of medicine. While the nature of the stimulus has not been found to be of great significance, the sequence of events initiated by it follow a rather consistent pattern, although certain of the characteristic changes or stages may not be clearly delineated in clinical observation. It is agreed, however, that the adrenal response and the profound changes induced in the adrenal secretory activity in all kinds of stress assume major importance in the ability of the body to withstand stress and in capacity for recovery.

Studies of the secretory activity of the adrenal during and after administration of trauma, or other stimulating agents, have shown that the secretory response is different with respect to the two major adrenal steroid complexes. After the injury, there is normally a marked initial increase in the production and excretion of 17-ketosteroids (mineralocorticoids and androgens of adrenal origin). This increase has generally been observed to reach its maximum 24 to 48 hours after the trauma and is briefly sustained. The production of 17-ketosteroids then falls to subnormal levels, which are maintained until recovery is achieved (7, 8, 12, 42). While the initial increase and subsequent depression in 17-ketosteroid production represent the normal course of events in the absence of previous adrenal stress or disease, the secretion of these steroids is different under conditions of stress in chronically ill or debilitated persons and in inanition. In these subjects, previous stress or disease has probably already depleted the adrenal reserve, and the response to additional trauma or stimuli may be absent or occur at an extremely low level; that is, increased 17-ketosteroid production does not signalize the response to trauma, nor does it necessarily induce any change at all (6, 7, 8, 12, 22, 45). In this respect these individuals present low resistance and decreased power of recovery.

The production of corticosteroid-like hormones of the adrenal complex (11-oxygenated steroids) follows a different secretory pattern. These substances are produced in great quantities during the periods of stress

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and convalescence. There is an initial rise in the levels of 11-oxygenated steroids at approximately the same time as the initial increase in 17-ketosteroid production. While the latter are soon being produced in subnormal amounts, corticosteroids continue to be produced in large amounts until convalescence and recovery are attained (41, 44, 46, 47, 48). Since the corticosteroid-like compounds are most intimately related to carbohydrate metabolism and gluconeogenesis, depletion of these substances in conditions of undue stress may lead to adrenal exhaustion and its undesirable sequelae.

It was thought that the postoperative difficulties observed in patients undergoing surgery with the additional stress of severe heat might be related to the adrenal response to the dual stimuli, and that the administration of an adrenal cortical preparation containing larger amounts of the 11-oxygenated adrenal steroids might be of value in ameliorating the condition. Although the efficacy of the various adrenal cortical preparations in combatting conditions of stress and associated phenomena is still controversial, it is generally agreed that they are useful in supportive treatment, but are not in themselves entirely adequate (14, 27, 28, 50). It is only recently, however, that a preparation containing more adequate amounts of the 11-oxygenated steroids has been available. These substances have been found to be more effective than steroids of the desoxycorticosterone series in ameliorating the effects of alarming stimuli in test animals (39, 40). Accordingly, the preparation selected for this study was an extract of hog adrenals (lipoadrenal cortex), since comparative studies have shown that hog adrenal preparations are more potent in correcting the disturbances in carbohydrate metabolism during the response to stress (20).

Women were selected for the study, since 17-ketosteroid production in them is probably entirely of adrenal origin (5, 13). The studies were begun in the summer of 1948, and most of the patients were operated upon during the summer months, although this community did not experience any severe heat waves during 1948 comparable to those during the summer of 1947. The subjects were a group of 20 unselected women who were undergoing major pelvic surgery for gynecological disorders. Ten of the patients received no adrenal cortical therapy and served as controls. The average age of the control group was 55.5 years, ranging from 33 to 71 years. Four of the patients in the control group had the diagnosis of carcinoma. The average age of the 10 test patients was 38.2 years, ranging from 29 to 56 years. There had been a diagnosis of carcinoma in 6 of the latter group. It is realized that the significant age difference and the preponderance of drastic surgical procedures in the subjects who received cortical extract may have somewhat occluded interpretation of the findings. Furthermore, certain of the patients were greatly alarmed by the diagnosis of carcinoma, and psychogenic stimuli undoubtedly were contributing factors in these instances.

METHODS

Blood and complete 24 hour urine specimens were collected 1 to 2 days preoperatively and daily for 7 to 8 days postoperatively. The collection of complete 24 hour specimens was facilitated by the use of indwelling catheters, and the urine was delivered directly by this means to iced containers kept constantly at the bedside. Hematocrits were determined (Wintrobe), chloride by the method of Schales and Schales, and blood urea nitrogen by the method of Archibald (1); 17-ketosteroid determinations were done by the method of Robbie and Gibson. All patients received the usual intravenous fluids and blood transfusions as needed.

Treatment with adrenal cortical extract was begun approximately 12 hours preoperatively. At this time the dose was 20 units intramuscularly. An additional 40 units was given immediately before operation, and 20 units 6 to 8 hours postoperatively. During the first and second postoperative days, 40 units were administered daily in 2 injections of 20 units each. Thereafter, for 2 days, the total daily dose was 20 units. The total amount of cortical extract administered was 200 units, which is a relatively small dose.

TABLE I.—POSTOPERATIVE FLUID EXCRETION IN SURGICAL PATIENTS WITH AND WITHOUT ADRENAL CORTICAL EXTRACT THERAPY

	Days	1	2	Total	Per cent excreted
Without	Intake	5700	2771	8471	45
	Output	1714	2121	3835	
With	Intake	2950	2350	5300	73
	Output	1781	2092	3873	

RESULTS

No untoward reactions were observed in any of the patients in either the treated or untreated group. However, there had been no marked climatic change during the time they were under observation. The average body temperature in the two groups was in every respect comparable, being 99.2 and 99.3 degrees, respectively, on the day of surgery and 100.1 degrees for both on the day following surgery. In a few instances the temperature rose to 101 degrees.

The total fluid intake among untreated patients was 15,461 cubic centimeters, and the total output was 9,826 cubic centimeters for 5 postoperative days (63 per cent). The treated patients had received a total of 10,925 cubic centimeters of fluid and excreted 8,925 cubic centimeters of urine (82 per cent) (Table I). The increased intake of the controls was significantly greater. The overall percentage difference in excretion for the two groups was only 19 per cent. The only significant difference in excretion is to be found during the first 48 hour postoperative period, when the percentage difference was found to be 28 per cent.

No very marked changes were observed in the blood chloride levels in any of the patients, the only variation being during the first 24 hours postoperatively. In the control group the average blood chloride was 331.6 milligrams per cent, a difference of 50.8 milligrams per cent in favor of the treated patients. The fact that the control patients had received an additional 1,585.5 cubic centimeters of fluids, consisting largely of glucose in saline (2:1), may mask the chloride values in this group, although the levels were within normal limits (365±15 mgm. per cent, Table II).

Probably the differences in fluid intake may be responsible also for the essentially unchanged hematocrit readings. The average values during the first postoperative period were 45.8 per cent and 46.4 per cent, respectively, and at no time reached abnormal levels (Table III).

Blood urea nitrogen values were also rather consistent in the two groups of patients, and were not significantly lower in the treated patients during the first postoperative period, averaging 9.75 milligrams per cent as compared with the average of 10.75 milligrams per cent of the controls (Table IV).

Preoperatively, 17-ketosteroid excretion in all patients was within the lower limits of normalcy, averaging 7.3 milligrams per 24 hours for both treated and untreated patients. The average preoperative excretion in the control patients was 5.0 milligrams per 24 hours, as compared with the average of 9.70 milligrams for the treated subjects. It is of interest that 2 of the latter patients had very high initial excretion levels (27.4 and 21.8 mgm./24 hours). Both of these patients were in highly exaggerated states of excitement, caused by the diagnosis of carcinoma and anxiety over the outcome of surgery. Determinations made on the urine of these patients several months postoperatively resulted in more normal values (14.2 and 9.6 mgm./24 hours, respectively). The significance of psychogenic influence on adrenal activity in certain individuals should not be underestimated in considering the effects of the procedure to be carried out.

There was the anticipated increase in 17-ketosteroid production during the first 48 hour postoperative period. Values averaged 8.1 milligrams per 24 hours in the controls, as compared with 12.7 milligrams per 24 hours in treated patients. The increase was comparable in the separate groups, but in the treated patients the initial increase was effected at a significantly higher excretion level, and the subsequent depression was not very evident, since on the fifth postoperative day the average excretion for the treated patients was 8.4 milligrams, as compared

TABLE II.—BLOOD CHLORIDE MILLIGRAMS PER CENT IN SURGICAL PATIENTS WITH AND WITHOUT LIPOADRENAL CORTICAL EXTRACT THERAPY

	Preop.	Surgery	1	2	3	4	5
Without	375.0	331.6	363.7	370.7	353.0	353.2	356.0
With	376.9	380.4	362.8	374.7	370.4	370.2	367.5

Normal (women) = 365 ± 15 mg. per cent (Schales)

TABLE III.—AVERAGE HEMATOCRIT PER CENT IN SURGICAL PATIENTS WITH AND WITHOUT LIPOADRENAL CORTICAL EXTRACT THERAPY

	Preop.	Surgery	1	2	3	4	5
Without	40.11	45.8	40.5	40.0	41.3	42.0	37.0
With	45.5	46.2	45.3	43.8	44.5	42.3	44.6

Normal (women) = 42 ± 5 per cent (Wintrobe)

with the average of 4.8 milligrams per 24 hours which was obtained for the controls. The average for the third, fourth, and fifth postoperative days (6.0 and 10.8 mgm., respectively) is, perhaps more representative of the actual status of adrenal function during the phase of depressed 17-ketosteroid excretion (Table V).

The treated patients included more poor risk patients, and they were subjected generally to more traumatizing procedures. Clinically, their course was better, their complications and complaints were less, and their recovery was more satisfactory to the operator.

DISCUSSION

In attempting to relate the status of patients subjected to the stress of surgery, moderately severe heat, and in some instances the debilitating effects of malignancy, to the general adaptation syndrome, certain pertinent observations during the course of the reaction will be reviewed. The observed changes have included reports of decreased volume of urinary output (17). Since, due to clinical indications, the fluid intake in the patients serving as controls in this study was significantly greater, evaluation of the actual fluid balance in the treated patients is difficult. The average total fluid administered to the untreated patients was 15,461 cubic centimeters during the first 5 day period of observation. The urinary output was 9,826 cubic centimeters, or 63 per cent of the intake. The treated patients during the same period of time received a total of 10,925 cubic centimeters of fluid, and the average total urinary excretion was 8,925 cubic centimeters, or 82 per cent. However, if the excretion values during the first 48 hour postoperative period are considered alone, the percentage excretion in the treated patients was significantly greater. The controls excreted a total of 3,835 cubic centimeters of urine during the 48 hours in which 8,471 cubic centimeters of fluid had been administered. The excretion rate was, then, 45 per cent of the total fluid intake. The treated patients during the same postoperative period received a total of 5,300 cubic centimeters of fluid and excreted 3,873 cubic centimeters of urine, or 73 per cent of the total intake.

While the hematocrit readings in all patients fell within normal limits, the change in the untreated patients during the first 24 hour postoperative period, when the figures are compared to the preoperative values in both groups, was the greater. The difference between the preoperative hematocrit determination and the reading during the first 24 hour postoperative period in the control group was 5.69 per cent, as compared with a difference of 0.7 per cent for the treated patients during the same postoperative period. This difference is of interest, since hemoconcentration in the control group was undoubtedly affected by the greater fluid intake, and a greater hemodilution may have been anticipated in these individuals, which is not borne out by the difference of 4.99 per cent between preoperative and postoperative levels.

The situation with reference to blood chloride is somewhat similar. During the initial stage of stress, the blood chloride is low and urinary excretion of chloride is decreased (18, 46, 47). The hypochloremia may then be followed by hyperchloremia during the countershock phase of the reaction (34). The very slight difference in blood chloride observed during the first 24 hour period in

TABLE IV.—AVERAGE BLOOD UREA NITROGEN MILLIGRAMS PER CENT IN SURGICAL PATIENTS WITH AND WITHOUT LIPOADRENAL CORTICAL EXTRACT THERAPY

	Preop.	Surgery	1	2	3	4	5
Without	13.7	11.6	9.3	8.8	10.3	9.9	9.5
With	11.4	10.9	8.6	7.7	9.9	9.7	9.8

Normal=8–18 mgm. per cent (Archibald)

TABLE V.—AVERAGE DAILY EXCRETION URINARY 17-KETOSTEROIDS MILLIGRAMS PER 24 HOURS IN SURGICAL PATIENTS WITH AND WITHOUT LIPOADRENAL CORTICAL EXTRACT THERAPY

	Preop.	Surgery	1	2	3	4	5
Without	5.0	7.9	8.4	8.1	8.7	4.6	4.8
With	9.7	12.5	13.0	12.4	13.0	11.0	8.4

Normal (women)=5–15 mgm./24 hrs. (Robbie & Gibson)

these patients (a difference of only 50.8 mgm. per cent) is probably masked by the administration of larger amounts of fluid to the control group. The difference is entirely without significance. It can only be said that the electrolyte balance with reference to chloride has been maintained. Facilities were not available for estimation of sodium and potassium. However, the behavior of these electrolytes during the response to trauma or stress are of great importance. Sodium is depleted during the initial stages but retained during countershock, when the body resistance is low (16), and there is loss of potassium from the tissues (9), with increased blood potassium levels (25), associated with increased urinary excretion of this electrolyte (10). During countershock there is marked retention of potassium (4).

Under these conditions there is evidence of deranged metabolism. Certain drugs, surgical procedures, and a variety of alarming stimuli are known to cause a decrease in basal metabolic rate, which, however, returns to normal during the countershock phase irrespective of continued stimuli (49). Nitrogen metabolism is most profoundly influenced. Blood urea nitrogen levels, under the impetus of alarming stimuli, are greatly increased (21, 49), as is the nonprotein nitrogen (25, 30, 32), and patients go into negative nitrogen balance (3) during the shock phase. Assuming blood urea nitrogen to be an index of protein catabolic processes, none of the patients in this series were at any time experiencing greatly accelerated protein catabolism. If the findings have any significance, in all the patients anabolic processes were predominant. However, under experimental conditions, protein catabolism and the related increased blood urea nitrogen have not been found to be mediated by corticosteroids, since in test animals adrenalectomy does not prevent its occurrence, and it is not to be supposed that the administration of these substances would influence the course of such processes in the human being (37).

Changes in 17-ketosteroid and 11-oxysteroid production during the course of the alarm reaction have already been mentioned (6, 7, 8, 12, 22, 42). Facilities did not permit evaluation of corticosteroid-like compounds in these patients, and only 17-ketosteroid determinations were done. The initial postoperative rise in 17-ketosteroid excretion was observed in all the patients, although the degree of the increase was comparable in the two groups. During the later period, when the excretion values are normally depressed, the decrease was perhaps more significant in the patients who did not receive adrenal cortical extract, in that the average excretion was very low (6.0 mgm.) during the third, fourth, and fifth postoperative days. The preoperative excretion level (9.7 mgm.) in the treated patients was initially more satisfactory, and the postoperative depression was maintained at a higher level, averaging 10.8 milligrams per 24 hours. When 17-ketosteroid excretion in the two groups of patients are considered separately, the degree of 17-ketosteroid response to the trauma of surgery was almost identical (about 3 mgm.), the only difference being that the response occurred at a higher level in the treated group; that is, the whole reaction never brought 17-ketosteroid production to critically low levels. Since the administered extract is comparatively rich in corticosteroids which are largely concerned

with carbohydrate metabolism, very marked increase in the excretion of mineralocorticoids and androgens was not expected.

The fact that none of these patients presented the frequently observed severe febrile reactions may mean that there was not sufficient heat stress imposed upon them. Much has been written concerning the biological effects of climate (26, 43), and the cold survival test for the evaluation of adrenal cortical activity is well known. Furthermore, exposure to intense heat produces shock-like symptoms in laboratory animals; and, in contrast to what is observed when other shocking stimuli are employed, the body temperature rises (33). Perhaps the best evaluation of the administration of the adrenal cortical extract is in the clinical course of the patients, which was eminently satisfactory. In most instances, those patients who were given the medication were subjected to rather more extensive surgery, and they stood the procedure well. When compared with untreated patients, subjected to at least equal surgical trauma, there was no doubt, clinically, that the postoperative course of the treated patients was more satisfactory than that of the untreated group. The urinary output was always adequate, the sense of well-being was greatly augmented, and recovery was attained without the occurrence of urinary retention, inanition, and, in some instances expected complications. While the dosage of adrenal cortical extract employed was comparatively small, the benefit, though not completely confirmed by the laboratory data, was evidenced by the clinical course of the patient. Larger doses may be safely employed, although the cost is still prohibitive for some patients.

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PRELIMINARY INVESTIGATION OF THE VALUE OF THE DIHYDROGENATED ALKALOIDS OF ERGOT IN THE TREATMENT OF EXPERIMENTAL FROSTBITE

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EXPERIENCE with frostbite and other cold injuries during World War II has emphasized the fact that little is known concerning these phenomena. Considerable controversy exists with regard to the pathogenesis of frostbite, and methods of treatment are numerous and varied. Lempke and Shumacker (7) contended that the gangrene which frequently follows frostbite is "due to the direct effect of cold on ischemic tissue with subsequent obliteration of the arterial tree by thrombosis." Their most effective treatment consisted of maintenance of peripheral vasodilatation through administration of tetraethylammonium chloride after initial rapid thawing. Immediate heparinization has also been shown to be of some value (4, 6, 11).

Recently, Finneran and Shumacker (3) conducted a series of experiments comparing the efficacy of rapid thawing alone and in combination with tetraethylammonium chloride, heparinization, and sympathectomy before and after freezing in the prevention of post-frostbite gangrene. They utilized rabbits, dogs, rats, and mice in their experiments, freezing the tails or feet of rats, the feet of dogs, the ears or feet of rabbits, and the tails of mice. Their studies indicated that the results with regard to tissue loss from the tails of mice, frozen at −15 degrees C. for 5 seconds and subsequently air-thawed, were extremely poor. When thawing was carried out rapidly by immersion in warm water (42°C.) the results in the various animals studied ranged from 11.1 per cent good to excellent results in the feet of dogs to 75 per cent excellent results in the ears of rabbits. Untreated animals, or those in which air-thawing was permitted, ranged from 0 per cent good results to a maximum of 15 per cent good to excellent results in dogs' feet. Heparinization combined with air-thawing after freezing the tails and feet of rats for 5 seconds at −20 degrees C. gave good results ranging from 19.5 per cent to 68.3 per cent. The results were not consistent with relation to whether heparinization was begun immediately or 3 hours after freezing. A combination of rapid thawing and heparinization was quite effective in the prevention of gangrene, and gave 96.7 per cent good to excellent results in rats whose feet were frozen for 5 seconds at −20 degrees C. Immediate administration of tetraethylammonium chloride gave 37.9 per cent good or excellent results in rats' tails and 93.5 per cent good or excellent results in rats' feet. Immediate administration of tetraethylammonium chloride was completely ineffective in the prevention of gangrene in rabbits' ears. When rapid thawing was combined with the immediate administration of tetraethylammonium chloride to rats with frozen feet, 100 per cent good or excellent results were obtained by these investigators. Sympathectomy carried out 10 days before freezing or immediately after freezing the ears of rabbits was completely ineffective in the prevention of gangrene. Sympathectomy immediately after freezing the feet of dogs was only moderately effective.

The present study, utilizing a mixture of three dihydrogenated alkaloids of ergot (dihydroergocornine, dihydroergocristine, and dihydroergokryptine), has been carried out to explore the possible clinical application of these drugs in frostbite inasmuch as the dihydrogenated alkaloids have been shown to have a vasodilator effect upon peripheral

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TABLE I.—TAIL LOSS 30 DAYS AFTER FREEZING*

Experimental group	Number in each group	Mean tail loss and S.E.m	Difference and S.E.d	Critical ratio $\frac{X}{\sigma}$ or Probability
Control	10	4.81± .26		
0.2 mgm. CCK	10	2.79± .13	2.02± .29	6.96 <0.001
0.4 mgm. CCK	10	1.33± .30	3.48± .39	8.92 <0.001
0.8 mgm. CCK	10	1.46± .18	3.35± .32	10.47 <0.001
0.2 mgm. CCK and heparin	10	2.62± .11	2.19± .28	7.80 <0.001
Control	10	4.81± .26		
			>1.52± .33	4.60 <0.001
Oral CCK (about 0.2 mgm.)	10	3.29± .20		
			>0.50± .24	2.10 0.036
0.2 mgm. CCK	10	2.79± .13		
			>1.16± .33	3.50 <0.001
0.4 mgm. CCK	10	1.33± .30		
			>0.13± .35	0.40 0.689
0.8 mgm. CCK	10	1.46± .18		
0.2 mgm. CCK	10	2.79± .13		
			>0.17± .54	0.31 0.757
0.2 mgm. CCK and heparin	10	2.62± .11		

*In this table and in Table II, the first five lines serve to compare the control values with each group of experimentals. In the second half of the table, the control group is first compared with the group given CCK-179 orally; the latter group is then compared with the group receiving 0.2 mgm. CCK-179 parenterally, and so on as indicated by the lines connecting average figures with the difference, critical ratio and probability values.

vessels (1, 10). In view of the observations of Finneran and Shumacker (3) and those of other investigators, it might have been anticipated that a drug with a primary vasodilator action would not be too effective in the treatment of frostbite when used in association with air-thawing. Nevertheless, the study was undertaken and it has yielded encouraging results.

METHODS AND MATERIALS

Sixty rats of Sprague-Dawley and Wistar strains have been used in this investigation. The ends of the tails were frozen while the animals were anesthesized with nembutal, by immersion in ether which was maintained at a temperature of −15 degrees C. with solid carbon dioxide. The distal 7 centimeters of each tail were kept in the cold ether for 60 seconds. Ten rats served as controls and the other 50 received the dihydrogenated alkaloids (CCK-179) in varying dosages. Ten animals were given heparin in addition to dihydrogenated alkaloids. Minimum treatment period was 10 days.

The tails were allowed to air-thaw and treatment was begun immediately, except in the case of the 10 control animals which received no treatment. One group of 10 rats received twice-daily injections of 0.1 milligram dihydrogenated alkaloids subcutaneously. A second group received the same dosage in the same manner, and at the same intervals, but each animal was given 0.8 milligram of heparin per day in addition to the dihydrogenated alkaloids. A third group of 10 animals received 0.1 milligram of dihydrogenated alkaloids at 6 hour intervals for a total dosage of 0.4 milligram per day. A fourth group of experimental animals was given dihydrogenated alkaloids (0.1 mgm. subcutaneously) at 3 hour intervals for a total of 0.8 milligram per day. Finally, a fifth group of experimental animals was given dihydrogenated alkaloids orally (about 0.2 mgm. per day). The drug in the last instance was placed in the drinking water which was available to the animals, and since there were several animals drinking from the same receptacle, only a rough approximation of the dosage could be made.

Skin temperature determinations in the distal and proximal areas of the tails of treated and untreated rats were obtained by means of a Brown 2-channel potentiometer. The skin thermopiles were loosely taped to the tail, one at the proximal and the other at the distal end, and the record was obtained over a considerable period of time in order to determine the average differences between skin temperatures of the two areas. The average differences within each group and between groups of animals, including the controls, were then subjected to statistical analysis (See Table II).

RESULTS

The results are summarized in Table I. Mean tail loss in each of the experimental and control groups of rats is shown, together with the standard error, and the statistical significance of the differences between groups and between each group and the controls is indicated.

Tail loss in the control animals averaged 4.81± 0.26 centimeters. This compared with a loss of 2.79± 0.13 centimeters in those rats given 0.1 milligram of dihydrogenated alkaloids twice daily. Slightly better results were

obtained when heparin (0.8 mgm. day) was combined with dihydrogenated alkaloids (0.2 mgm. day); in these animals, the mean tail loss was 2.62 ± 0.11 centimeters.

When dihydrogenated alkaloids were given alone at 6 hour intervals for a total daily administration of 0.4 milligram, the mean tail loss was only 1.33 ± 0.3 centimeters. Increasing the daily dosage to 0.8 milligram, divided into 0.1 milligram injections at 3 hour intervals, did not improve the results over that obtained with half this dosage. The mean tail loss in these animals was 1.46 ± 0.18 centimeter.

Oral administration of dihydrogenated alkaloids did not give satisfactory results when administered in the manner described. Mean tail loss was 3.29 ± 0.2 centimeters. More accurately controlled oral administration of the drug might produce much better results.

Photographs of distal portions of the tails of all the control and experimental rats, after tissue loss had reached its maximum in each case, are shown in Figure 1.

Comparison of the skin temperatures of proximal and distal portions of the tails in control and experimental rats (experimental in the sense that they were given dihydrogenated alkaloids revealed statistically significant differences between control and treated animals (Table II). It was possible on the basis of such skin temperature determinations to predict the effectiveness of the treatment with regard to probable loss of tail tissue.

TABLE II.—TEMPERATURE DIFFERENCES RECORDED ON THE 2ND TO 5TH DAY AFTER FREEZING

(Proximal and Distal Ends of Tails)

Experimental group	Number in each group	Mean temperature difference and S.E.$_m$	Difference and S.E.$_d$	Critical ratio $\frac{X}{\sigma}$	or Probability
Control	10	3.52 ± .24			
0.2 mgm. CCK	10	1.82 ± .31	1.70 ± .39	4.59	<0.001
0.4 mgm. CCK	10	2.73 ± .52	0.79 ± .57	1.38	0.177
0.8 mgm. CCK	10	1.45 ± .24	2.07 ± .34	6.08	<0.001
0.2 mgm CCK and heparin	10	2.18 ± .28	1.34 ± .37	3.26	<0.001
Control	10	3.52 ± .24			
Oral CCK	10	2.86 ± .36	> 0.66 ± .57	1.15	0.250
0.2 mgm. CCK	10	1.82 ± .31	> 1.04 ± .47	2.21	0.028
0.4 mgm. CCK	10	2.73 ± .52	> 0.91 ± .60	1.52	0.134
0.8 mgm. CCK	10	1.45 ± .24	> 1.28 ± .57	2.21	0.028
0.2 mgm. CCK	10	1.82 ± .31			
0.2 mgm. CCK and heparin	10	2.18 ± .28	> 0.36 ± .42	0.857	0.390

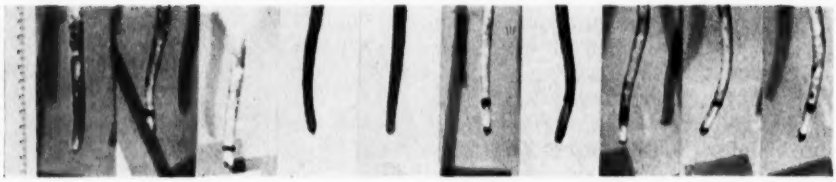
DISCUSSION

Exposure of the body or parts of the body to cold normally results in a pronounced constriction of the blood vessels. According to Lewis three separate reactions are responsible for the vasoconstriction. One is a local response and is a direct effect upon the blood vessels of low temperature; the second is a local reflex vasoconstriction mediated through the central nervous system; the third is a general persistent vasoconstriction which results from the effect of the cooled blood upon the hypothalamic vasomotor center. In exposure to cold of sufficient severity and duration, these reactions contribute greatly to tissue anoxia.

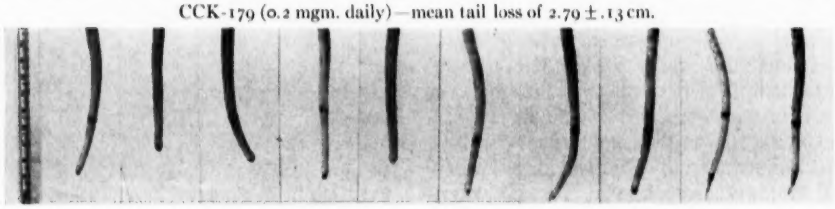
Release of vasoconstriction and its attendant ischemia may indeed be of prime importance in the treatment of frostbite and other conditions brought about by exposure to cold. The dihydrogenated ergot alkaloids appear to act through adrenergic blockade, resulting in a reduction of sympathetic tone and a consequent relaxation of the vessel wall. Nickerson, however, proposes that the response is brought about by a depressive action on the brain stem. Regardless of the mode of action of the drug, an enlarged peripheral arterial and capillary bed follows treatment with dihydrogenated alkaloids. This has been demonstrated in normal animals through continuous recording of skin temperatures before, during, and subsequent to administration of dihydrogenated alkaloids.

In 1917, Lake, working with a large variety of tissue cultures of man and other animals, arrived at a critical environmental temperature of −6 degrees C., below which tissue damage was irreparable. In view of this, our results in rats' tails frozen at −15 degrees C. for 60 seconds are encouraging. Statistically, the reduced tissue loss in all the experimental groups as compared with the control series was significant. For example, in the group receiving the smallest daily dose of dihydro-

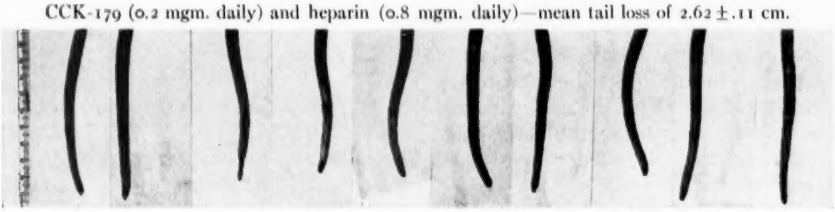
Control—mean tail loss of 4.81 ± .26 cm.



CCK-179 (0.2 mgm. daily)—mean tail loss of 2.79 ± .13 cm.



CCK-179 (0.2 mgm. daily) and heparin (0.8 mgm. daily)—mean tail loss of 2.62 ± .11 cm.



CCK-179 (0.4 mgm. daily)—mean tail loss of 1.33 ± .30 cm.

Fig. 1 (*Legend on opposite page*).

genated alkaloids, the probability was only 7 in 100,000 that such a difference between tail loss in experimental and control rats could be due to chance alone. This probability became less with each increase of daily dosage up to 0.4 milligram of dihydrogenated alkaloids. Above this point, improvement was not significantly greater than in those rats receiving smaller amounts of the drug (Table I). This may be due to the fact that a functional saturation point has been reached at this level of dosage.

Table I indicates that the better results in the group receiving heparin and 0.2 milligram of dihydrogenated alkaloids than in the control group were due largely to the action of the vasodilator (CCK-179) and not of the anticoagulant (heparin). The difference in tail loss between the group receiving 0.2 milligram of dihydrogenated alkaloids and 0.8 milligram of heparin per day and the group receiving only 0.2 milligram of dihydrogenated alkaloids per day was not statistically significant.

We found evidence for direct correlation of the temperature differences between the proximal and distal ends of the tails with the amount of necrosis and final tail loss that occurred (Table II), but a much greater number of animals must be studied before it will be possible to express this relationship mathematically.

CCK-179 (0.8 mgm. daily)—mean tail loss of 1.46 ± .18 cm.

CCK-179 oral (about 0.2 mgm. daily)—mean tail loss of 3.29 ± .20 cm.

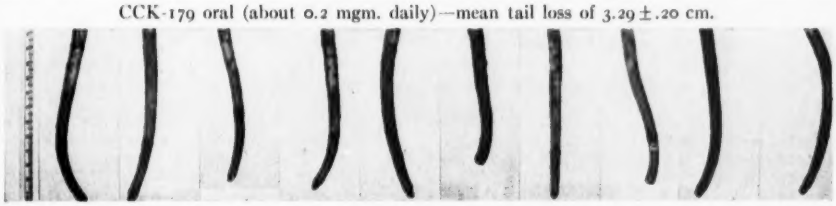


Fig. 1. Photographs of tails of control and experimental rats after the loss of tissue had reached its maximum in each individual case. The extent of immersion of each tail in ether at −15 degrees C. is indicated by the black mark. It will be noted that the greatest loss of tissue occurred in the control animals, and the least loss in the group which received 0.4 milligram of dihydrogenated alkaloids per day, administered in 0.1 milligram doses at 6 hour intervals. Increasing the dose to 0.8 milligram per day (0.1 mgm. every 3 hours) did not improve the results.

During World War II a unique type of cold injury came into prominence. This injury, a variety of Lake's "true frostbite" is that which is incurred by airmen at altitudes of 20,000 to 27,500 feet. Davis, Scarff, and associates report that this type of injury "differs from the common frostbite as greatly as the 'Birds-Eye' foods differ from cold storage foods." Aside from the fact that a condition of anoxia may prevail during high altitude cold injury (inadequate oxygenation has been thought [10] to augment cold injury), this type of frostbite resembles in several respects that produced experimentally in our studies. Both are the result of exposure to extreme degrees of cold for a comparatively short period of time. The degree of cold is the most important contributing factor; gangrene is not secondary to venous stasis, maceration of tissues, malnutrition, or other factors which may be concerned in the immersion syndrome, for example.

Release of vasoconstriction may be of importance in the treatment of high altitude frostbite. If so, to be effective, it must be obtained early, before thrombosis has taken place.

SUMMARY

Exposure of the body or parts of the body to cold normally results in a pronounced constriction of the blood vessels. Prompt release of such vasoconstriction with relief of ischemia is of prime importance in the treatment of frostbite and other conditions brought about by exposure to cold. The present study, utilizing a mixture of three dihydrogenated alkaloids of ergot (dihydroergocornine, dihydroergocristine, and dihydroergokryptine), has been carried out to explore the possible clinical application of these drugs in frostbite inasmuch as the dihydrogenated alkaloids have been shown to have a vasodilator effect upon peripheral vessels. Sixty rats of Sprague-Dawley and Wistar strains have been used in this investigation. Following exposure of the distal 7 centimeters of their tails to −15 degrees C. for 60 seconds, 50 rats received the dihydrogenated alkaloids (CCK-179) in varying dosages, and the other 10 animals, which received no therapy, served as controls. Ten animals were given heparin in addition to dihydrogenated alkaloids. It was possible, on the basis of skin temperature determinations, to predict the effectiveness of the treatment with regard to probable loss of tail tissue. The improvement over the controls of each treated group was statistically significant. There is indication that the improvement in the group receiving both heparin and dihydrogenated alkaloids was due largely to the action of the

vasodilator and not to that of the anticoagulant. The dihydrogenated ergot alkaloids may well prove to be of value in the treatment of high altitude frostbite.

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TECHNIQUE OF VAGOTOMY AND GASTROENTEROSTOMY IN THE TREATMENT OF DUODENAL ULCER

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EXPERIENCE has shown that gastroenterostomy alone is an unsatisfactory treatment for duodenal ulcer and that vagotomy alone is also unsatisfactory. Only about 50 per cent of patients subjected to gastroenterostomy alone obtain satisfactory results (4), and evidence of recurrent ulceration occurs in about 11 per cent of patients subjected to vagotomy alone (6). But each of these operations plays a part in controlling duodenal ulcer and in our 4 years' experience, the two operations, when combined, act synergistically to give better results than can be obtained by gastric resection or any other form of surgical treatment (2, 5).

If gastroenterostomy is protected by an adequate vagotomy the incidence of recurrent ulceration is exceedingly low and if the denervated stomach is drained by a properly functioning gastroenterostomy side effects of the operation are few (4). The mortality rate of vagotomy combined with gastroenterostomy has been less than 1 per cent (2 deaths in 265 patients operated upon at the Cleveland Clinic for duodenal ulcer). But if good results are to be obtained the vagotomy must be sufficiently complete to protect the gastroenterostomy stoma against recurrent ulceration and the gastroenterostomy be so placed as to drain the atonic denervated stomach.

With the combination of a satisfactory vagotomy and a well functioning gastroenterostomy, retention after operation rarely is observed, Levin tubes can be removed on the first day after operation, diet can be increased rapidly, and the majority of the patients can be discharged from the hospital within a week after operation, eating a simple diet. After 6 weeks they may eat, drink, and smoke as they please. The longer term results appear to be equally gratifying and in our experience have been superior to those following gastric resection both in respect to control of the ulcer and in side effects (1).

Although our experience with vagotomy and gastroenterostomy has been most satisfactory, many surgeons have not been gratified either with the immediate or the later results following vagotomy combined with gastroenterostomy in the treatment of duodenal ulcer (7). One of the factors causing this difference in opinion may be differences in the selection of patients for operation. If, for example, a surgeon elects to treat half of the patients with complicated duodenal ulcer by vagotomy and gastroenterostomy and the other half by resection of the stomach, the results are not comparable unless the cases are alternated or selected for operation by the same criteria. If vagotomy and gastroenterostomy have been reserved for those patients who show minimal objective evidence of ulcer and if gastric resection has been employed for those who have large craters and severe manifestations of the disease, the results in the group subjected to vagotomy would be very poor because included in this group would be most of the patients with functional disorders of the gastrointestinal tract (3).

A second cause for reported poor results following vagotomy is the fact that in many of the published reports vagotomy was used alone, without gastroenterostomy or pyloroplasty (7).

A third cause for reported poor results has been a tendency to consider gastric ulcer and duodenal ulcer together (7) in spite of the fact that the two diseases are generally considered to be different in etiology and in spite of the fact that vagotomy is rarely advocated in the treatment of gastric ulcer under any circumstances (2). Even marginal ulcers which occurred in patients with an enteroenterostomy below the stoma have been included as failures of vagotomy (7) despite the fact that this would be the expected result in this type of Mann-Williamson preparation.

From the Cleveland Clinic and the Frank E. Bunts Educational Institute.

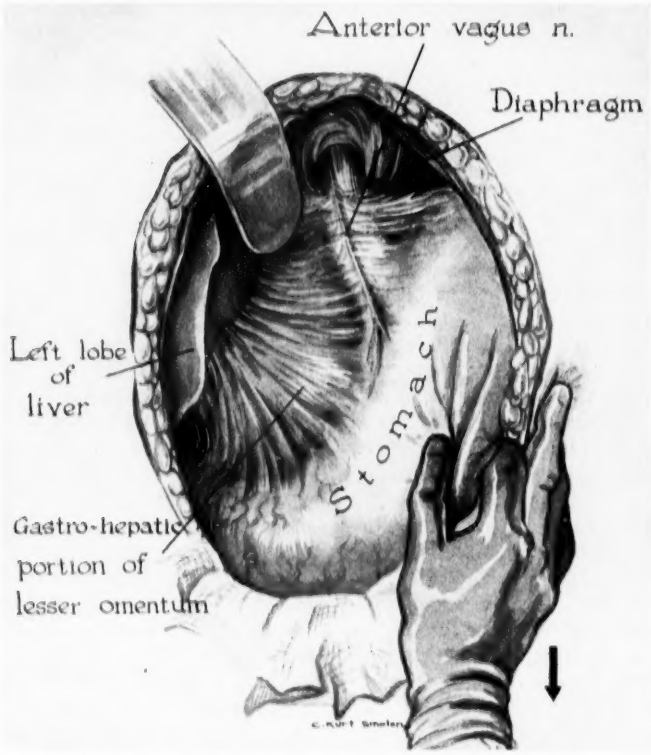

Fig. 1. Identification of anterior vagus trunk. The liver is lifted forward with a retractor and the stomach is pulled downward to tense the vagus nerves. These are readily palpable and can be picked up on nerve hooks.

Although many of the differences in opinion as to the value of vagotomy and gastroenterostomy may be explained by divergent methods of selecting patients for operation and analyzing results, it is apparent that there remains a basic difference in end results obtained by different surgeons.

It is possible that these differences may be explained by differences in the technique employed. Since the end results depend so much upon the completeness of the denervation and upon the proper emptying of the denervated stomach it is perhaps desirable to emphasize the technical aspects of the procedure.

TECHNIQUE OF VAGOTOMY

The key to locating the vagi is downward traction of the stomach which immediately tenses the nonelastic vagi and renders them easy to palpate amid the elastic structures of the muscle, areolar tissue, blood vessels, and peritoneum on and about the esophagus. If a filament does not go to the stomach it will not be stretched and will not be palpable. But if it does go to the stomach, even hair-like fibers of the vagus nerve, which would be difficult if not impossible to visualize, stand taut and are easily felt (Fig. 1).

Since the purpose of vagotomy is to denervate the stomach, it is not necessary to isolate or expose the esophagus, nor is it necessary or desirable to reflect the left lobe of the liver. Isolation and visual dissection of the esophagus at the level of the diaphragm is difficult and may be dangerous, whereas it is easy and safe to locate the vagi by sense of touch and

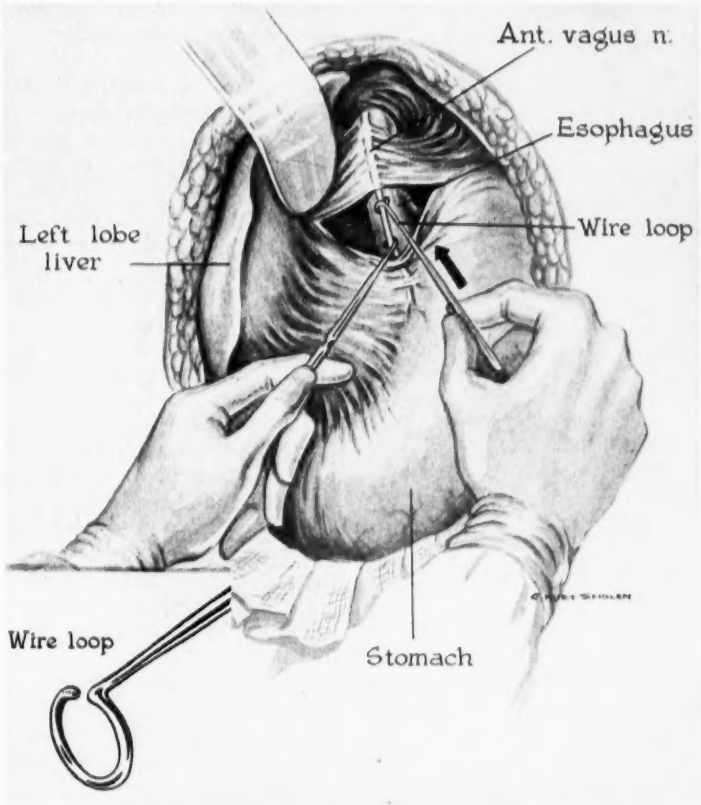

Fig. 2. Isolation of vagus trunk with nerve hook and nerve stripper. After the nerve is identified by palpation it is lifted on a nerve hook and 2 or 3 inches of the nerve are isolated with the nerve stripper prior to resection.

to resect an inch or two of each nerve without isolating the esophagus. The level of resection is at or above the level of the diaphragm and I believe the denervation is more complete than when the esophagus is mobilized and the fibers are located by inspection.

Preparation for operation. Either general anesthesia or high spinal anesthesia supplemented by pentothal may be used. The stomach should be emptied by a Levin tube before operation and the tube left in place. This assures an easily manipulated stomach and aids in the identification of the esophagus.

Exposure. A midline incision is less vascular and easier to open and close than a left rectus incision, and it also affords a higher and hence a better exposure. It extends from the umbilicus to the xiphoid.

Before proceeding with vagotomy the abdomen should be explored, and the surgeon should examine with special care the stomach, duodenum, gall bladder, and esophageal hiatus. It is unwise to perform a gastric operation before vagotomy because soiling from the gastric operation may result in contamination of the vulnerable mediastinum and subdiaphragmatic space during the vagotomy. Moreover, if a satisfactory vagotomy cannot be accomplished, surgeon may elect to perform a gastric resection rather than a gastroenterostomy.

The left lobe of the liver does not interfere with exposure of the vagus if a broad Deaver

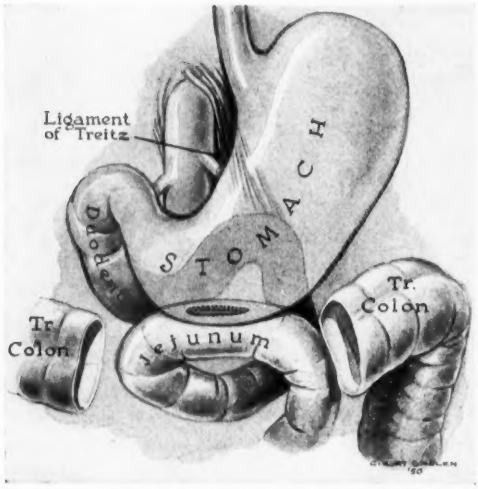

Fig. 3. Posterior gastroenterostomy is placed as near as possible to the greater curvature and on the most dependent portion of the denervated stomach.

or malleable retractor is inserted under the lobe to lift it forward (Fig. 1).

Identification of the vagus. The surgeon stands on the right side of the table. The anterior vagus is quite constant in its location and usually can be found with little or no difficulty. The stomach is grasped in the right hand with a moist tape and retracted downward, while an assistant retracts the liver anteriorly to expose the lower part of the esophagus. By palpation with the left hand the operator can identify the Levin tube in the esophagus. Firm downward traction is then exerted on the stomach in such a way as to stretch the esophagus. The vagus nerve is nonelastic and stands out like a violin string, palpable and often visible beneath the peritoneum (Fig. 1). As soon as the nerve is identified by palpation with the index finger of the left hand and with the finger still in place to identify the vagus, the traction on the stomach is delegated to an assistant who maintains it while the peritoneum overlying the nerve is incised and the nerve is picked up on a long nerve hook. Its identity is unmistakable, and as soon as it is isolated it can be proved to be the vagus by following it upward through the esophageal hiatus in the diaphragm. The blood vessels of the stomach do not course in this direction nor does the esophageal hiatus transmit any other structure from the thorax to the abdomen (Fig. 1).

The nerve is isolated by blunt dissection with a special nerve stripper (resembling a tiny fascia stripper) which is passed through the diaphragm and preferably higher in order to isolate the nerve and remove all accessible branches (Fig. 2). An open Moynihan clamp is then placed on the nerve and is slid upward, pushing peritoneum and diaphragm ahead of it and the nerve is clamped just above the former level of the diaphragm. The nerve is again clamped just above the stomach, and divided below both clamps, the intervening segment being removed with the lower clamp. The upper clamp, whose chief function is to hold away the overlying diaphragm, is removed without ligation, as the vagus does not bleed and Dragstedt has shown that it does not regenerate.

After completion of the anterior vagotomy the forefinger of the left hand is inserted through the hole in the peritoneum and is directed into the areolar space lying to the right of the esophagus. The stomach is again pulled downward by the right hand and the posterior vagus is located by palpation as a tense cord lying posterior and to the right of the esophagus. Occasionally it appears to be more to the right of the esophagus than posterior and may be surprisingly far away from it. While an assistant pulls the stomach downward to tense the nerve and toward the ceiling to lift it forward and render it more readily palpable, the nerve is identified by the index finger of the left hand, is picked up by a nerve hook, and is isolated and resected, as in the case of the anterior nerve. It is important to make certain that it passes upward through the esophageal hiatus since there are vessels posteriorly that could be confused with the vagus if its course through the hiatus is not checked. Traction is again placed on the stomach and the esophagus and the surrounding area is palpated carefully for any additional filaments coming down from above the diaphragm. It is not necessary to reconstruct the peritoneum.

Attention is next directed to whatever operation on the stomach is desirable to prevent gastric retention. Pyloroplasty, gastric resection, and gastroenterostomy each has its place,

but gastroenterostomy usually is the best means of draining the denervated stomach.

TECHNIQUE OF GASTROENTEROSTOMY

The denervated stomach is devoid of peristalsis, tends to dilate, and hangs down into the pelvis so that it may not empty satisfactorily even if the pylorus and duodenum are patent. Such a stomach must empty by gravity rather than by peristalsis. Gastroenterostomies that are placed in the middle of the posterior aspect of the stomach, those whose efferent loops are near the lesser curvature, and those that are made toward the cardia do not drain the denervated stomach effectively because they are not placed at its most dependent part.

Since one must rely on gravity, rather than on peristalsis to empty the denervated stomach the stoma should be at the most dependent part. Usually this is just to the left of the reflection of the transverse mesocolon over the pylorus. The incision extends to the left for 2 inches exactly parallel to the greater curvature and as close to it as possible. The jejunum is attached to the stomach in an antiperistaltic fashion with its efferent loop pointing to left. The point of anastomosis is about 6 inches from the ligament of Treitz (Fig. 3).

Immediate results. Gastric retention of a degree sufficient to prolong hospitalization beyond 10 days or require readmission to the hospital occurred in only 3 of the last 80 consecutive cases in which this technique has been employed. In one, the gastrojejunal anastomosis was isoperistaltic instead of antiperistaltic. In this case the sutures between the stomach and mesocolon pulled out allowing herniation of the jejunum through the rent in the mesocolon and causing obstruction. It was necessary to readmit the patient to the hospital and revise the stoma 10 days after the patient had been discharged with no symptoms of retention. Another patient with retention was an obese man who developed an omentitis with massive edema and necrosis of the entire omentum which wrapped itself around the jejunum and constricted it. A third patient developed an unexplained transitory retention which subsided spontaneously after 10 days. The median postoperative hospital stay in these 80 cases has been 7 days.

The longer range results analyzed over a period of 1 to 3 years after operation have been reported elsewhere and remain satisfactory. Eighty-seven per cent of the patients operated upon have obtained good results and only 4 per cent have had recurrence of ulcer-like symptoms or objective evidence of ulcer (1).

SUMMARY

1. Neither vagotomy alone nor gastroenterostomy alone is a satisfactory method of treating duodenal ulcer.

2. A properly functioning gastroenterostomy and an adequate vagotomy, when combined, act synergistically to afford the safest and most effective surgical treatment for patients with complicated duodenal ulcer.

3. Most of the so-called "side effects of vagotomy" are the result of gastric retention and can be avoided by combining vagotomy with a well placed gastroenterostomy.

4. The gastroenterostomy should be placed exactly at the most dependent part of the denervated stomach so as to allow drainage by gravity.

5. The gastroenterostomy should be posterior and antiperistaltic. It should be placed parallel to the greater curvature, as close to it as possible, and at its most dependent point.

6. The vagotomy must be complete enough to protect the vulnerable gastroenterostomy from recurrent ulceration.

7. A technique of vagotomy is described in which the nerves are put on tension and are located by palpation.

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THE NEUROVASCULAR MECHANISM OF THE STOMACH AND DUODENUM

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TO relegate body mechanism to physiology, structural units to anatomy, and never to combine the two is to parcelate a mass of factual knowledge that makes sense only when combined. The subject matter under consideration might be spoken of as belonging in the field of "functional anatomy," rather than in either of the subjects. We are concerned with neurovascular mechanisms and with what these mechanisms do to alter temperatures regionally. Temperature in a selected region at a chosen time depends upon the number of vessels, the calibers of these vessels relative to the calibers of others, the rate of flow, the linear pressure and oxidative processes in the tissues and heat loss by various and sundry means.

The gross angioarchitectural features of the stomach are well known, but the study of the reactions of the stomach and duodenal vessels has barely reached the horizon of modern investigation. This study deals with each anatomical entity, the right gastric artery, the left gastric artery, the right and left gastroepiploic arteries in their individual intricate relationships with the cardiac-fundic as well as the pyloric regions of the stomach.

On observing the omentum of dogs, it was seen that the capillaries fired in groups; that is, first one unit showed the blood moving along at a rapid rate, whereas the segment in juxtaposition was at rest. The blood appears to come to rest or nearly so. The flow at times is very sluggish. This action is like gunfire. Some investigators feel that this is a transfusion of one area to another area within an organ or tissue, or from one organ or tissue to another. An attempt is herein made to correlate the operation of these factors with the etiology of ulcers.

The mucous membrane of the gastrointestinal tract is as much an external surface as is the skin covering the body; therefore, a burn of the mucous membrane may cause a body reaction similar to that of a burn of the skin surface. In 1887, Decker produced mucosal ulcers in dogs by feeding them gruel at 62 degrees C. Cooks have a high incidence of ulcers because they continually taste hot foods (1, 5, 6).

Vascular changes in a gastric stoma during different emotional states have been observed by Wolf. Trueta (21) demonstrated a reflex shunting of blood flow within the kidney. Necheles (15, 7, 8, 9) postulated that rapid intragastric temperature excursions, as caused by swallowing hot liquids or hot foods, might temporarily cause vasoconstriction and local anoxia. Inasmuch as in most cases of ulceration of the stomach and duodenum the pathology is restricted to a limited area, the possibility of related vascular changes was considered. Usually ulcers of the stomach involve the pyloric segment along the lesser curvature, those of the duodenum occur within the first inch of the duodenal cap and nearly always on either the dorsal or ventral wall. Pursuant to the hypothesis of vascular changes in tissues and organs, the vessels of the stomach were injected either with red cinnabar or bismuth oxychloride in water, in order to visualize the angioarchitectural features and the passive behavior of the vessels during injection. The arteries were injected in a pulsatile fashion simulating the action of the living heart in injecting the same vessels with blood. Krogh (10) in 1922, showed that when the blood vessels of muscles in the fresh state were perfused with contrast material, it was difficult to obtain a complete and comprehensive injection. Microscopic examination of the x-ray plate of such specimens revealed the fact that of the large number of capillaries supplied by its source arteriole, a minority had been injected in spite of high pressure. This is selective because the power to accommodate to intra-

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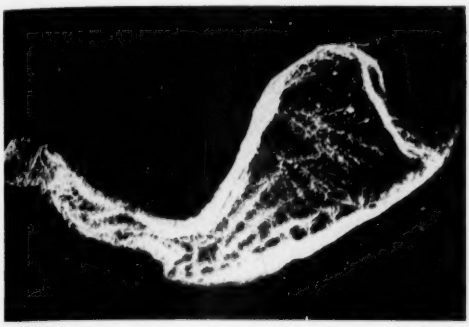

Fig. 1. Roentgenogram of cinnabar injected human stomach showing coarse vessels in the cardiac-fundic area traversing the long axis of the organ. Note that the vessels on the pyloric area are much smaller in caliber and that they run longitudinally.

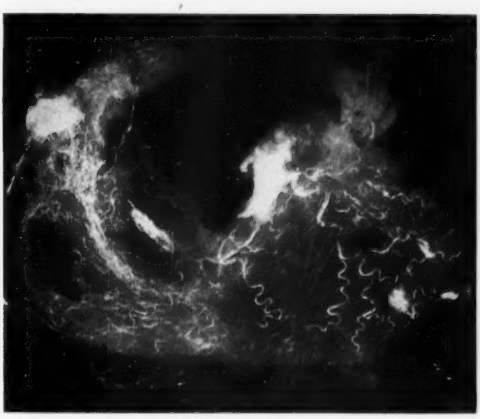

Fig. 2. X-ray photograph of human stomach showing the coarse fundic vessels. The circumferential anastomosis can readily be seen. This picture clearly shows the abrupt turn the left gastric assumes in its return course to the cardiac-fundic area. The vascular pattern in the pyloric area, because of the small caliber of the vessels, makes a finer and denser network.

vascular pressure is idiopathic to the vessels of different tissues. This fact becomes obvious when it is realized that the distensibility of a blood vessel is directly dependent upon its size and more so on the medium in which it resides. This behavior of the vessels prevented the free flow of cinnabar, resulting in imperfect injections which could be falsely interpreted.

Stimulation of the peripheral stump of the right vagus causes a greater flow of pepsin and hydrochloric acid than does stimulation of the left vagus. This difference in secretion suggested a change in the regional blood flow. It would be necessary to determine whether this change consisted in a more rapid or less rapid flow. The effect was much as though the blood were static, or almost static, over such a period of time. This was also indicated by Krogh (11). Krogh pointed out, in addition, that, when the blood flowed at an unusually slow rate, the oxygen present was used up and, therefore, led to a regional tissue anoxia (12). Lillehei, Dixon, and Wangensteen, have shown that ulcers of the upper gastrointestinal tract are more rapidly induced because of local ischemia of the mucosa from vasoconstriction. Davis and Ivy (3) assumed that altered blood supply may be concerned in the evolution of gastric ulcers, gastritis, or carcinoma (16, 17).

As Trueta (22) demonstrated the blanching of the kidney by stimulating the proximal stump of the sciatic nerve, it was found repeatedly that stimulating the distal stump of the right vagus caused a blanching of the pylorus. In these experiments, however, the effect was produced directly upon the segmental area of vessels and not by reflex reaction.

MATERIALS AND METHODS

Some of the stomachs used were specimens from postmortem examinations and surgical procedures performed in local hospitals. The causes of death or reasons for surgery varied as in any urban hospital. Other specimens came from dogs, rabbits, and Macaca mulatta monkeys.

In preliminary work, some of the specimens were injected with red cinnabar and roentgenographed (Figs. 1 and 2). More recently bismuth oxychloride as well as neosilvol was used. The particles of bismuth oxychloride are smaller in size than cinnabar but still large enough to remain on the arterial side when injected through a selected artery. This substance packs well in even the smallest vessel and is an excellent substance for radiologic studies, except that it is white in color and accordingly does not stand out as well as cinnabar in the gross specimen. Neosilvol is a colloidal iodide, and goes readily from the arterial to the venous side. It is not opaque to the type of x-rays that were used and its color is nearly that of the tissue. It proved of no advantage

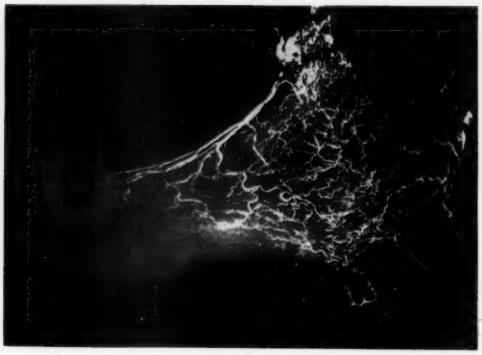

Fig. 3. Radiopaque cinnabar injected through the left gastric artery shows the blood vessels in the cardiac-fundic area. Note the absence of contrast material in the pyloric region. The sharp turn to the cardiac-fundic region and the anastomosis between the lesser and greater curvatures are very pronounced. Extrusion of contrast material at cut splenics and esophageal vessels makes for puddling.

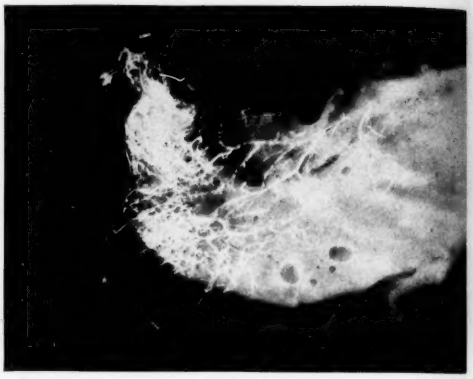

Fig. 4. Roentgenogram of human stomach. Injection of the right gastric artery through the hepatic artery filled the vessels in the pyloric region and the vascular pattern in the cardiac-fundic area was not visualized. The vessels in this area are smaller and course toward the pyloric sphincter.

and its use was discontinued. All the blood vessels in a specimen were injected, the contrast radiopaque medium being used successively in each of the gastric arteries.

One hundred stomachs were divided into two groups: half of them were to be injected through the left gastric artery, and the other half through the right gastric artery. All of those injected through the left artery showed a clearly defined vascular pattern in the cardiac-fundic area but not in the pyloric region.

Fig. 5. Roentgenogram of stomach from a patient with a diagnosis of acute pancreatic necrosis. The injection was made through the left gastric artery. The cinnabar failed to enter the vessels in the pyloric region except for a vessel in an inflammatory band.

Figure 3 is an example of this type of injection. The other 50, injected through the right gastric artery just beyond its derivation from the hepatic artery, showed a vascular pattern in the pyloric region and not in remainder of the stomach. Figure 4 shows the contrast material in the blood vessels of the pyloric region.

Some of the stomachs regionally injected were from patients who had expired from an intra-abdominal inflammatory disease, such as acute pancreatic necrosis or appendicitis with perforation and generalized peritonitis. These showed the typical patterns previously described but also had blood vessels present in the inflammatory bands. In Figure 5, the solitary band can be seen traveling from the greater to lesser curvature in the pyloric area.

The next step was to determine the effect of vagal stimulation on the regional vascular pattern. Monkeys and dogs were anesthetized with ether or nembutal and either cinnabar or bismuth oxychloride in water was injected through the descending thoracic aorta so as to visualize the gastric vascular pattern. Other monkeys and dogs used as controls were injected with cinnabar or bismuth oxychloride in water through the descending aorta without nervous stimulation. In some of the experiments the vagotomy was performed through a midline incision between the xiphoid process and the umbilicus. Artificial respiration was

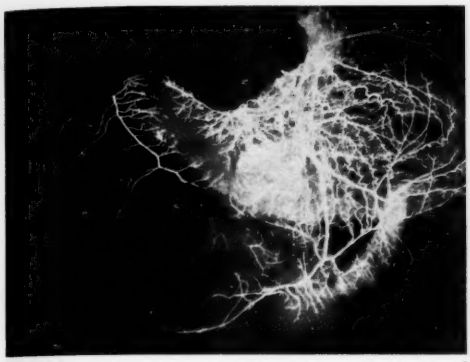

Fig. 6. Roentgenogram of stomach from a dog in which the cut distal stump of the right vagus was stimulated just above the diaphragm. The cinnabar was injected through the descending thoracic aorta. Note the incomplete filling of the pyloric portion of the stomach and the extensive arterial network in the cardiac-fundic area. The vessels visualized are coarse and traverse this region from the lesser to the greater curvature.

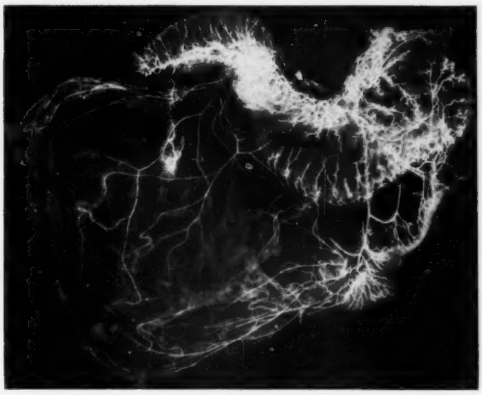

Fig. 7. Roentgenogram showing stimulation of the left vagus was done subdiaphragmatically. The bismuth oxychloride was introduced through the descending thoracic aorta. Stimulation was done with a Goodwin stimulator using a saw-tooth wave, frequency 20, descending phase 20 sigma, voltage 8. The vascular pattern is deficient in the fundic and cardiac areas. The pylorus appears as a solid mass of vessels. This is also true along the lesser curvatures. The vessels of the duodenum are visible and show the circumferential pattern with the vessels entering from the mesenteric border. The bismuth oxychloride because of its size (much smaller than cinnabar) makes a compact injection. Cinnabar would have been much better for this study as many of the very small vessels would not have been filled, therefore a more contrasting picture would have been produced.

given to all animals on which the transthoracic approach was used. On these anesthetized animals, the right vagus was cut. The distal stump was stimulated with an inductorium (1.0 MH) or with the Goodwin stimulator with the use of a saw-tooth wave, frequency 20, descending phase 20 sigma, voltage 8. This was done until the demise of the animal. Because of the fatigability of the synapse, excessive constant stimulation of the distal stump of the vagus resulted in a reduction of the quantity of pepsin-hydrochloric acid secreted as compared with a similar period of time when interrupted stimulation was used. The stomachs of some of the animals were cannulated and sampled to observe the type of secretion present prior to and after stimulation of the cut right vagus nerve. The stomach of each animal contained a thick viscid colorless fluid before stimulation. After stimulation, the contents were highly acid, strongly peptic, and watery. The gastric fluid content was considerably increased. The vessels of the stomach were injected via the descending aorta. The time interval was such as to allow for a more complete injection as demonstrated by Swindle and by Krogh in 1922. It was important to cut the vagus below the cardiac plexus in order to avoid direct vagal action on the heart. Study of the roentgenogram showed that the greater part of the pylorus was devoid of the injected bismuth oxychloride or cinnabar, whereas the remainder of the stomach showed a normal vascular pattern. The major blood vessels along the greater and lesser curvature in the pyloric region can be seen; but, along the "magenstrasse," no pattern is apparent, as shown in Figure 6. Figure 7 is a photograph of the injected stomach from a dog whose left vagus was stimulated subdiaphragmatically. Comparison of Figure 6 with Figure 7 makes the absence of intravascular contrast material in the pyloric region as shown in Figure 6 more striking.

One of the human stomachs injected through all the vessels presented a peculiar vascular pattern. The roentgenogram was typical of a specimen from a right vagal stimulation experiment or one of the stomachs injected only through the left gastric artery. This specimen like all the others used was opened and inspected and on all of the folds of the pyloric region punctate ulcers were seen. The opened

pylorus with its ulcers looked like the tentacles of an octopus.

To get an exact cast of the blood vessels of the stomach, plasket No. 56 was used. This substance is incredibly hard and transparent and it holds its shape. The transparency of this material equals that of the finest crystal. It is colored red as the material is injected into the arteries. This is a thermosetting type of plastic; that is, it hardens under heat. Perhaps due mainly to its viscosity, its flow stops on the arterial side. In injection molding, used for thermoplastic material, the plastic is fed into a heating chamber; and, after preheating, it is forced under pressure into the blood vessels. The heating tends to eliminate air bubbles. The use of this method proved very instructive, as it showed the abnormal bends the vessels assumed when a pressure of 150 millimeters of mercury or higher was used. The picture obtained here by use of plasket was definitely abnormal. The vessels would never function in this manner in a normal living individual. The specimens were digested free of organic material by various dilutions of acids, but the best method found in the present investigation was to wet them and expose them to the action of maggots. For demonstration purposes, the pictures were of some value to prove that pulsatile injections within normal blood pressure range was best and that the actual vascular arrangement was not that seen when excessive force was used to urge contrast material into blood vessels.

The use of plastics in blood vessel demonstration is known as injection molding. This method presents some characteristic problems. These problems were solved by the trial and error method. The vessels were washed out by the use of bovine plasma, as India ink or water produced fractured patterns. The plastic was activated by the use of a catalyst. The mixture was thoroughly stirred and a red dye added. Fifteen drops of the aniline dye to 5 tablespoonfuls of the mixture gave an ideal arterial color. The syringe, rubber tubing, and cannula were all coated with carnauba wax to prevent adherence of the plastic to the equipment. The wax had to be applied hot and the coat made a very thin film to avoid freezing the syringe or injection of the excess wax into the blood vessels. Paraffin was not used as it acts as a catalyst to the plastic. So much stress is placed on technique because different patterns can be produced by the use of different contrast media and different pressures.

Noer and Derr state that their earlier injections of blood vessels were performed by the use of pressure of 200 and 250 millimeters of mercury pressure and that when they approximated the more nearly normal arterial pressure of 100 to 150 millimeters they could see no significant variations. To obviate muscular contractions in dog intestine, they injected a dog that had been killed the day before and again saw no demonstrable difference in the end result despite absence of intestinal contraction. The use of bovine plasma to wash out the vessels prior to injection with contrast material proved efficacious.

To attempt to visualize the gastric vessels in animals with marked vasodilation, acetylcholine chloride and etamon chloride (tetraethyl-ammonium chloride) were used prior to injection of the bismuth oxychloride (14). These specimens did not deviate sufficiently from the normal controls to merit comment. An attempt was made to show the course of the injected material through the vascular bed of the stomach. This was done by working the blood out of the arteries by perfusing with bovine plasma. Bismuth oxychloride in water was then injected into the arteries and an x-ray exposure taken every second. The x-ray technique was: 60 milliamperes at 1 second, 40 inch distance, 40 kilovolts, Bucky film. Five exposures were usually necessary to complete the visualization of the entire vascular bed of the stomach. The right and left gastric arteries were injected simultaneously.

To substantiate the statement that the vascular pattern of an organ to some extent at least depends upon the contrast material used, some stomachs were injected with cinnabar (Fig. 8) and then washed free of this medium by retrograde perfusion through the venous system and reinjected with another type of radiopaque material (bismuth oxychloride). This contrast pattern may be seen in Figure 9. Cinnabar in water did not show as many of the very small arteries as did bismuth oxychloride or protargol in the same specimen.

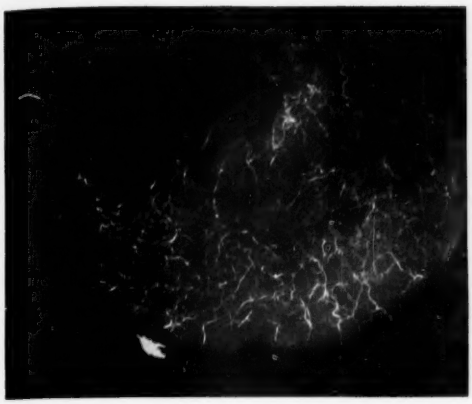

Fig. 8. The vessels of this human stomach were injected with cinnabar. Then by injecting .85 per cent saline through the veins, the cinnabar was washed out of the arteries. The washing was repeated until the solution returned clear. This can be performed easily by using an intravenous bottle and allowing the specimen to wash over night. The next figure shows the same stomach injected later with bismuth oxychloride.

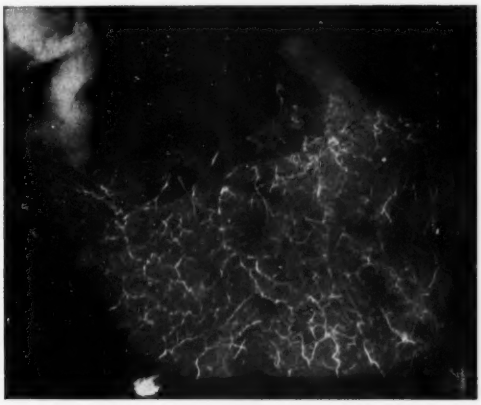

Fig. 9. This is the same specimen as in Figure 8, except that the injection material used this time was bismuth oxychloride. The x-ray and photographic technique were the same as for Figure 8. Notice the greater number of vessels demonstrated. Because of the large number of small vessels injected, the pattern appears blurred. This contrast shows the importance of the media which is used in vascular studies.

In another specimen, one segment of vessels was injected with cinnabar in water and the remainder of the vessels were perfused with bismuth oxychloride.

LABORATORY FINDINGS

On close study of the specimens with the binocular microscope, it was readily seen that the mesenteric vessels enter the muscularis layer of the stomach much as the ureter enters the urinary bladder. The vessels run but a short distance through this layer and then become sandwiched between the mucous membrane and the muscularis layers in what is known as the loose areolar area. From this rather loose vascular bed, the main blood vessels then send branches into the mucous membrane and back into the muscularis that they had perforated. It was further seen that the architecture of the vascular bed in the cardiac-fundic area of the stomach differed from either the pyloric or duodenal areas. The blood vessels in the cardiac-fundic area appeared relatively large and coarse. They traversed the stomach circumferentially from the lesser curvature to the greater curvature and arboresced parallel with the lesser and greater curvatures. In the pyloric area, however, on inspection of the roentgenograms, the vessels were relatively fine and either followed the cardiac-fundic pattern or ran in the direction of the long axis of the organ. If the vessels ran with the long axis, the secondary branches traveled perpendicularly to the lesser and greater curvatures. In the duodenal area, the vessels were larger than those in the pyloric area but were much smaller than the main vessels of the cardiac-fundic region. These vessels course along the circumference of the lumen and had but a few branches as shown in Figures 1 and 2.

DISCUSSION

Anatomically, the arteries of the stomach arise from two large arterial arcuates along the lesser and greater curvatures. From here, they are distributed to the ventral and dorsal walls from the loose areolar vascular highway situated between the muscularis and mucous membrane.

The project at hand attacks the physiologic anatomy of the stomach from a totally different point of view, the aim being to show the anatomy as a functional unit. Nonidez and Windle state that blood vessels, except the very smallest, are always full of blood in the living anatomy. This has been demonstrated

as being at variance with the change in the vascular pattern of the pyloric area of the stomach when the distal stump of the right vagus is stimulated.

The vascular pattern of one portion of the stomach was visualized by injecting the left gastric artery as shown in Figure 3, and another injecting the right gastric artery (Fig. 4). Constant phasic stimulation with a weak current of the distal stump of the right vagus (Fig. 6) just above the diaphragm produced a different vascular pattern from that of the side of the stomach under control of the left vagus (Fig. 7). Since the vessels in all the layers of the gastric wall, both anterior and posterior, were devoid of the contrast material, it is apparent that this is not a shunting phenomenon within the organ but diversion of the blood to other organs, such as the liver or pancreas. This might be a regular shift in an advanced state of digestion and not an internal shunting of shock as suggested by Barclay and Bently. It gives the organs added blood at that point in the process of food disintegration necessary for the elaboration of the digestive juices which they produce.

The Lovén reflex might be the answer to the periodicity of the symptoms of the ulcer patient. To date, no better explanation of the cyclic complaints of the ulcer patient has been advanced.

SUMMARY

This has been a study of the peculiarities of the gastric blood supply on a functional basis. It has also been a study of the relationship of the regional blood flow.

Stimulation of the peripheral right vagus stump changes the vascular pattern in the pyloric end of the stomach and necessarily alters the blood flow within the related organs. Stimulation of the distal stump of the right vagus below the cardiac plexus alters the amount, the type, and the acid-pepsin quality of the gastric juice. This has been a study of the different radiopaque contrast materials as well as gradients of pressure used in injecting passive blood vessels. It is interesting to note that Ivy, Grossman, and Bachrach in their book on peptic ulcers stated, "The best way to account for the circumscribed nature of the acute ulcer caused by acid or any other ulcerogenic agent is by assuming a local disturbance of the blood supply."

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TOTAL COLPOCLEISIS FOR PELVIC EVENTRATION

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PROLAPSE of the vagina or cervical stump following total or supravaginal hysterectomy is a most incapacitating and distressing condition. These unhappy and greatly restricted patients are in great need of a satisfactory and dependable operative procedure to rehabilitate them. When I was first confronted with this problem some 15 years ago, it became apparent that there was no specific operative procedure that was entirely adequate for the relief of this distressing situation. The criteria for a completely satisfactory operation for this condition demanded: first, complete relief of the associated incapacitating symptoms, and, second, permanency of the support and nonrecurrence of any degree of the prolapse.

Standard types of repair, repair with abdominal suspension of the vagina or cervical stump, or the Le Fort's operation have not fulfilled these criteria. Because of dissatisfaction with the results of these procedures, I developed a totally obliterating vaginal operation termed total colpocleisis. The first patient in this series was operated upon in 1937. Since that time I have used this procedure in 30 cases. As experience increased it became apparent that this operation was also indicated in patients with extreme degrees of uterine prolapse associated with huge enteroceles (or cul-de-sac hernia) and complete loss of support. In this series there were 11 of this latter type of case.

The single disadvantage of this operation is the permanent and complete obliteration of the vagina and the loss of the marital function of the vagina. Actually this has not proved to be a point of importance in this series. In most of these patients, because of their age and the long-standing severe degree of the prolapse, this loss of marital function was of no importance to them, and even in the few cases in the younger age group, these patients were so miserable and confined by their symptoms that both the patient and her husband, even after careful explanation of the procedure, were more than willing that the operation be performed provided permanent relief of these symptoms could be promised. With this procedure it has been possible to assure them of an excellent and permanent result and, without exception, these patients have been completely relieved of their distressing, incapacitating symptoms and have been exceedingly grateful and satisfied with the result.

Because of the extent and duration of the prolapse in these patients, they should be prepared for 48 hours in the hospital, chiefly to give the patient some needed rest and reduce the local congestion of the tissues to facilitate operation and reduce blood loss. This time should also be utilized for a careful soap and water preparation of the prolapsed mucosal tissues and to prepare the lower bowel by catharsis, enemas, and a low residue diet.

TECHNIQUE OF OPERATION

The operation itself is carried out under spinal pontocaine anesthesia and with the patient in the usual lithotomy position. The bladder is emptied and the entire perineal region carefully prepared with ether and zephiran. If the cervix is present it is grasped with a tenaculum, or if a total hysterectomy has been done, the scar representing the apex of the vagina is identified and is likewise grasped with a tenaculum. The mucosa on the anterior aspect of the completely prolapsed vagina, which on this aspect represents an almost complete eventration of the bladder, is opened (Fig. 1, a) from the cervix or vaginal apical scar to a point just below the urethra. These mucosal flaps are elevated from the bladder and the walls of the vagina laterally as far as the labial margin. The controlling tenaculum is then elevated, exposing the posterior aspect of the prolapsed vagina which represents an eventration of the rectum or, in many instances, a large enterocele. The posterior fourchet is grasped with double hooks on either side of the perineum, the mucosa excised transversely at the muco-

TABLE I.—SUMMARY OF CLINICAL DATA IN 30 CASES

Case	Age, years	Marital state	Date of previous operation	Type of previous operation	Symptoms	Duration, years	Date of colpocleisis	Complications	Result
1	54	M	1918	Supravaginal hysterectomy	Prolapse, frequency	10	12- 3-37	None	Excellent
2	68	W	1915	Supravaginal hysterectomy	Prolapse, frequency, dysuria	23	3- 2-38	None	Excellent
3	63	D	1906 1924	Supravaginal hysterectomy Suspension	Prolapse	34	6- 3-40	None	Excellent
4	53	W	1935	Total hysterectomy	Prolapse, pain	5	9- 5-40	None	Excellent
5	57	M	1939	Supravaginal hysterectomy	Prolapse, pain, bleeding	1	10-22-40	None	Excellent
6	71	W	1921 1940	Supravaginal hysterectomy Le Fort's operation	Prolapse, vaginal bleeding	20	5-31-41	None	Excellent
7	65	W*			Prolapse, frequency, incontinence (enterocele)		6-26-41†	None	Excellent
8	65	M	1921	Supravaginal hysterectomy	Prolapse, dysuria, frequency	12	9- 4-41	None	Excellent
9	45	M	1935	Total hysterectomy	Prolapse, pain, dysuria, frequency	6	9- 8-41	None	Excellent
10	71	W	1937	Total hysterectomy	Prolapse, pain, frequency	4	10-15-41	None	Excellent
11	59	S	1934	Vaginal hysterectomy	Prolapse, dysuria, frequency	1	12-10-41	None	Excellent
12	75	W	1936	Total hysterectomy	Prolapse, pain bladder and rectum	6	3-19-42	None	Excellent
13	72	W	1921	Panhysterectomy	Prolapse, stress, incontinence	10	4-29-43	None	Excellent
14	64	M	1925	Panhysterectomy	Pain, dysuria, frequency		4-18-45	None	Excellent
15	72	M*			Prolapse, pain, frequency, bleeding (enterocele)	8	7-11-45†	None	Excellent
16	60	M	1931	Panhysterectomy	Prolapse, bloody discharge	6	7-24-45	None	Excellent
17	63	M	1906 1916 1934	Repair Repair Repair	Prolapse, pain, frequency, incontinence (enterocele)	10	5-31-46†	None	Excellent
18	70	W	1945	Vaginal hysterectomy	Prolapse, pain (enterocele)	1	7- 6-46	None	Excellent
19	71	W*	1908	Suspension	Prolapse, pain, discharge	5	9-11-46†	None	Excellent
20	51	M	1942	Panhysterectomy	Prolapse, pain	2	12-18-46	None	Excellent
21	76	W	1912	Pelvic operation	Prolapse, stress, incontinence	20	1- 6-47†	? Cardiac infarction	Excellent
22	58	W*			Prolapse, frequency (enterocele)	10	2-19-47†	None	Excellent
23	62	W	1943	Panhysterectomy	Prolapse, pain	25	9-26-47	None (history of "milk leg," bilat., superior femoral venous ligation at operation	Excellent
24	59	M	1935	Total hysterectomy	Prolapse, pain, frequency, incontinence	12	10- 3-47	None	Excellent
25	62	Separated*			Prolapse, urinary frequency (enterocele)	4	9-21-48†	None	Excellent
26	62	M*			Prolapse, pain, frequency, bleeding (enterocele)	14	10-21-48†	Thrombophlebitis, diabetes	Excellent
27	65	M*			Prolapse (enterocele)	6	12-30-49†	None	Excellent
28	54	M*	1933 1949	Suspension Repair	Prolapse (enterocele)	1	2-15-50†	None	Excellent
29	59	W	1941	Supravaginal hysterectomy	Prolapse	1	4-29-50	None	Excellent
30	69	M*			Prolapse, frequency, dysuria	3	7-26-50†	None	Excellent

*No previous hysterectomy but patient had uterine prolapse and enterocele
†Vaginal hysterectomy plus colpocleisis

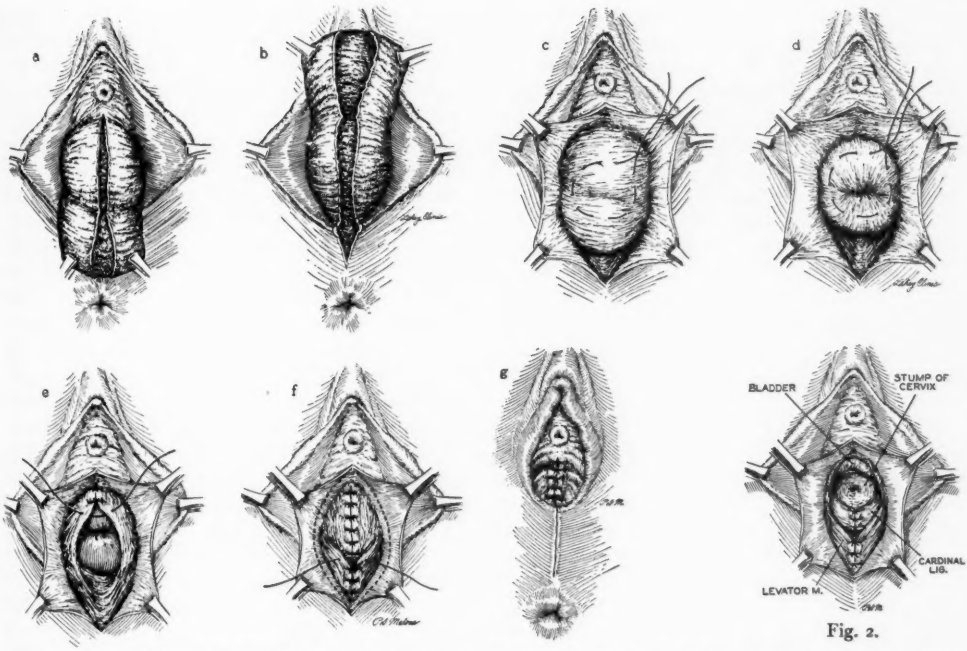

Fig. 1. Technical steps of total colpocleisis. a, Incision in the mucosa of the anterior aspect of the prolapsed vagina. b, Incision in the mucosa of the posterior aspect of the prolapsed vagina. c, Placement of first purse-string suture about the apical vaginal scar. d, Using the first purse-string suture as a focal point, a series of purse-string sutures is placed to invert the bladder and the rectum and reduce the prolapse. e, Plication of the pelvic fascia. f, Plication of the levator and transverse perineal muscles to obliterate the vagina. g, Completed operation after closure of mucosa.

Fig. 2. Plication of the cardinal ligaments *behind* the cervix rather than anterior to it for the control of enterocele.

cutaneous border of the perineum, and the posterior mucosa elevated as in a standard perineorrhaphy. The mucosa is then incised in the midline to encircle the cervix or vaginal apical scar and to connect with the anterior mucosal incision. This forms two mucosal flaps resulting from a midline incision extending from the perineum (Fig. 1, b) to the urethra and elevated laterally from the sides of the bladder, rectum, and the vaginal walls, being freed laterally as far as the mucocutaneous borders of the vagina. The cervical stump if present is then amputated as high as possible and, using the apical vaginal scar as a focal point, a series of purse-string sutures is placed (Fig. 1, c and d) to invert progressively the bladder and rectum and thereby reduce the prolapse. This likewise brings the bladder and rectum back to a normal relationship in the pelvis when viewed in a sagittal section.

The urethra is then plicated. The pelvic fascia, the levator and transverse perineal muscles are brought together (Fig. 1, e and f) to obliterate the vagina completely, the levator muscles and fascia being plicated beneath the urethra to construct a solid, strong, permanent support for the bladder and rectum.

The excess of the lateral vaginal mucosal flaps is removed and the mucosa closed (Fig. 1, g) leaving only a vestige of the vagina—a small (2 cm.) dimple just below the urethra to provide an unobstructed flow of the urinary stream from the urethral orifice. The perineal skin is closed with a fine subcuticular suture.

OTHER PROCEDURES

A modification of this procedure has been utilized effectively in patients with complete procidentia associated with huge enteroceles. This marked degree of herniation of the cul-

de-sac has also been extremely difficult to cure by standard procedures. In those patients with a lesser degree of prolapse but who have an associated marked enterocele, I have used a modified Manchester-Fothergill procedure, amputating the cervix and plicating the cardinal ligaments *behind* the amputated cervical stump (Fig. 2), rather than anterior to it as in the standard procedure, in order to prevent recurrence of the cul-de-sac hernia.

The cases with the marked degrees of procidentia associated with huge enteroceles are, however, best managed by vaginal hysterectomy, plication of the cardinal and broad ligaments and total colpocleisis.

CONCLUSION

It is evident that with these specific indications and careful selection of cases for total colpocleisis there will not be a large number of patients in whom this procedure should be used. In my own experience, in a period of 15 years it has been used in 30 cases. Table I shows the clinical data of this series of patients. It will be noted that the age ranges from 45 to 75 years. Many of these patients had had previous attempts at repair, including standard types of colporrhaphies, abdominal suspension of the stump, Le Fort's operation, but with recurrence and progression to the extreme degrees of distressing prolapse. It is also apparent that, since the incidence of total prolapse of the vagina and its related organs after hysterectomy is not great, this would indicate that the majority of surgeons and gynecologists are exercising care in the technical details of suspension of the cervical stump or vagina after hysterectomy. The fact that this distressing condition still occurs, however infrequently, justifies a plea and calls specific attention to the importance of these details of suspension during hysterectomy. Since all these patients were operated on without a serious complication or mortality, all have obtained excellent permanent results and over half have been followed for 5 years and others considerably longer, these excellent results have completely justified the application of this procedure in this selected group.

EXPERIMENTAL PRODUCTION OF INTERVENTRICULAR SEPTAL DEFECTS

Certain Physiologic and Pathologic Effects

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THE recent advances in surgical corrections of cardiovascular malformations have made it desirable to study in the laboratory the physiology and possible methods of correction of these anomalies. Because they do not occur in experimental animals with any considerable frequency, experimental techniques must be devised by which the anatomic and physiologic alterations found in the human cardiovascular system may be closely simulated.

HISTORICAL REVIEW

Holman and Beck (7, 8) created interventricular septal defects in dogs by introducing a knife into the left ventricle and piercing the interventricular septum, preferably in its midportion. An incision was made in the septum toward the apex of the right ventricle in the longitudinal axis of the heart. These authors reported producing defects in 10 dogs, weighing 10.4 to 18.4 kilograms. Four of the dogs lived 7 weeks to 8 months with defects measuring from 26 to 30 millimeters in circumference (8.2 to 9.5 mm. in diameter); 1 lived 5 months with two defects, 16 and 10 millimeters in circumference (5.4 and 3.1 mm. in diameter, respectively); 1 lived 23 days but the site of the defect was completely healed. Four dogs died in 36 hours or less with defects greater than 30 millimeters in circumference (9.5 mm. in diameter). In the surviving animals Holman and Beck noted a systemic arterial hypotension which was gradually, over a period of months, restored to normal by a progressive increase in the total blood volume. There was an obvious thickening of the wall of the right ventricle and a definite hypertrophy as measured by weight.

Eppinger and Gross reported creating in dogs interventricular septal defects which were 4 to 6 millimeters in diameter. The defects were made by introducing the cardiovalvulotome of Cutler and associates into the left ventricle through its apex. Preoperative and postoperative determinations of the cardiac output by the direct Fick method revealed that the total output of both ventricles is greater after the production of such a communication between them than before. The shunt of blood was estimated to be 30 to 50 per cent of the left ventricular output, leading to an increase in the amount of blood flowing through the pulmonary artery and a decrease in the systemic blood flow. Roentgenograms taken before and after production of the lesion showed a marked postoperative increase in the size of the right ventricle. Information was not given concerning the length of survival of the animals with patent defects.

Murray has described attempting the closure of congenital interventricular septal defects in 3 human patients with apparent success in 2 of them. After animal experimentation and a study of human cardiac anatomy, he devised an operation in which a strip of fresh autogenous fascia lata was passed, with the aid of manual palpation, from anterior to posterior across the left ventricular surface of the interventricular septum approximately over the site of the defect. The fascia lata was placed under slight tension and fixed in position by epicardial sutures at both ends. In his opinion this effected at least a partial closure of the defects. In 2 cases this was further suggested by moderate clinical improvement. The third patient died of atelectasis of the left lung 1 week after operation.

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Abridgment of thesis submitted by Dr. Griffin to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

At necropsy the suture was in a satisfactory position.

Recently, Galante and co-workers reported producing and closing interventricular septal defects in dogs by a cardiotomy, stating that the defects remained patent for several weeks. Surgical closure of the defects was performed with strips of autogenous fascia lata. No evidence was presented that these defects would not eventually heal spontaneously.

PRODUCTION OF INTERVENTRICULAR SEPTAL DEFECTS IN DOGS

The instrument. Since the size of the septal defect is an important factor in its physiologic effects, it was considered desirable to devise an instrument which would excise a piece of septum of a specific diameter. After much experimentation the final instrument evolved was based on the principle of a trocar (Fig. 1). It was introduced into the right ventricle of the heart and thrust through the muscular portion of the septum (Fig. 2). There were three sharp prongs on the edge of the trocar-head designed to engage the tissues of the left ventricular aspect of the septum. These prongs prevented the return of the instrument through the perforation in the septum and aided in securing the septal tissue for more effective excision. The sleeve was screwed down over the shaft slowly, for the advancing edge of the sleeve was the cutting edge. When the cutting edge impinged on the trocar-head, the excision of the piece of septum of a desired diameter was complete and the piece was then contained within the instrument, preventing it from becoming an embolus.

The operative technique. The chest of the anesthetized dog was entered through an incision into the right fourth intercostal space. A longitudinal incision was made in the pericardium parallel and ventral to the right phrenic nerve. The site of the incision into the wall of the right ventricle was immediately below the atrioventricular sulcus and parallel to the vessels which usually diverge perpendicularly from the right coronary artery in this sulcus. Before the incision was made, traction sutures of No. 1 linen on straight needles were placed parallel to the site of the proposed incision. Each suture was passed deeply into the myocardium two or three times to provide good fixation and then the ends were tied together 3 or 4 inches from their points of insertion into the myocardium. A single No. 000 silk suture on a ¾ inch curved needle was placed at the superior pole of the anticipated incision and tied in place, to be used for the quick repair of the ventricular incision. The two traction sutures were crossed one through the other and the incision into the right ventricle was made, large enough to accommodate the instrument. The instrument was inserted in a closed position into the right ventricle and the crossed traction sutures were pulled snugly around the instrument by the assistant, thus preventing the ejection of blood around the instrument from the ventricular incision. While the instrument was held in a fixed position in the heart, the sleeve was unscrewed to the maximum, unsheathing the shaft, and the defect was created as described previously. The introduction of the little finger of the surgeon into the right ventricle before insertion of the instrument proved a valuable aid in ascertaining the position of the septum. This maneuver was done without adverse effect and it was also used to check the existence of the defect. When the patency of the defect was established, the incisions in the wall of the right ventricle, the pericardium and the thoracic wall were closed.

Technical difficulties. Because the method was essentially a blind procedure it is apparent from the anatomy of the septum and related structures that there were hazards associated with the operation. Injury to the tricuspid, mitral or aortic valves, production of fatal cardiac arrhythmias, injury to the wall of the left ventricle opposite the septum, or excision of a portion of the septum without creation of a communication between the ventricles were possible results of the operation. All of these hazards were minimized by the development of a proper technique for performing the puncture and excision.

ACUTE EXPERIMENTS

In 5 dogs under pentobarbital sodium anesthesia acute interventricular septal defects were created with an instrument 10 millimeters in diameter. A Cournand catheter was

TABLE I.—DATA OBTAINED BY DIRECT FICK METHOD FROM DOGS WITHIN 60 MINUTES AFTER CREATION OF INTERVENTRICULAR SEPTAL DEFECTS WITH 10 MILLIMETER INSTRUMENT. THE PERCENTAGE OF BLOOD ENTERING THE LEFT VENTRICLE WHICH WAS SHUNTED INTO THE RIGHT VENTRICLE IS SHOWN

Dog	Oxygen content, vol. per 100 c.c.			Blood flow, liters per min.			Shunt per cent
	Atrial	Pulmonary	Femoral	Systemic	Pulmonary	Shunt	
A	15.4	19.8	22.4	2.03	6.12	4.09	67
B	10.5	13.8	14.5	0.79	4.51	3.72	83
C	11.9	13.4	14.1	4.07	7.10	3.03	43
D	14.5	15.9	17.9	1.80	3.02	1.22	41
E	8.6	15.3	18.4	0.60	1.76	1.16	66

TABLE II.—PREOPERATIVE AND POSTOPERATIVE MEAN PRESSURES IN THE CAROTID ARTERY (MM. OF MERCURY), PULMONARY TRUNK, RIGHT VENTRICLE AND RIGHT ATRIUM (CM. OF WATER) IN 5 ANIMALS WITH ACUTE INTERVENTRICULAR SEPTAL DEFECTS CREATED WITH THE 10 MILLIMETER INSTRUMENT

Dog	Carotid artery, mm.		Pulmonary trunk, cm.		Right ventricle, cm.		Right atrium, cm.	
	Before	After	Before	After	Before	After	Before	After
A	130	130	13.5	21.7	7.9	22.7	−2.3	8.7
B	160	90	9.2	15.0	6.5	13.0	−1.8	6.0
C	124	100	12.6	20.1	9.0	22.2	+2.2	8.0
D	148	110	10.8	18.9	7.2	17.8	−2.6	5.8
E*	Normal	110	Normal	26.5	Normal	15.0	Normal	4.5

*No preoperative controls taken on this animal.

introduced into the external jugular vein and passed with the aid of roentgenoscopy into the heart. The cardiac output and amount of blood shunted through the defects were determined by the direct Fick method, using the Van Slyke-Neill manometric method and a cuvette oximeter for whole blood to measure the oxygen content of blood samples. The latter instrument was developed by Wood and calibrated empirically for use in dogs by Takaro in this laboratory. Because it has been doubted (9, 12) whether it is possible to obtain a true mixed venous blood sample from the right atrium of a dog by cardiac catheterization, this matter was investigated (6). If it is not possible to obtain a true mixed venous sample from the right atrium, the accuracy of quantitative intracardiac shunt determinations in dogs by the direct Fick method would be at best speculative. It was found in normal dogs that the difference between the oxygen content of blood samples taken several minutes apart from the pulmonary trunk and right atrium was no greater than the difference between the oxygen content of blood samples taken several minutes apart from the pulmonary trunk.

No attempt was made to compare the cardiac output of the animals before creation of interventricular septal defects with the cardiac output of the same animals after the defects were produced. Even without the operative procedure the cardiac output of dogs was observed to fluctuate widely over a period of time from the effects of pentobarbital sodium anesthesia alone (6). Any cardiac output determined before the operation as a control would be an unreliable standard.

The systemic flow, pulmonary flow, and amount and percentage of blood shunted from the left ventricle into the right ventricle in these animals is shown in Table I. In none of the animals with interventricular septal defects was there evidence of right-to-left shunt of blood. In these experiments it was established in the first hour following creation of a defect with an instrument 10 millimeters in diameter that 41 to 83 per cent of the blood entering the left ventricle was shunted into the right ventricle. The changes in mean pressure, as shown by mercury and water manometers, occurring in the carotid artery, pulmonary trunk, right ventricle and right atrium of these dogs are presented (Table II).

CHRONIC EXPERIMENTS

Relation of the size of the defects to survival. To determine the largest possible defect in the interventricular septum which a dog could tolerate, instruments of four different sizes were employed. They were 12, 10, 8, and 5 millimeters in diameter. Adult mongrel dogs weighing 8 to 12 kilograms were used initially. The weight range of the dogs used in later

experiments was raised to 15 to 23 kilograms so that larger hearts were subjected to the procedure.

The number of dogs in which each instrument was used and the results obtained are shown in Table III. It was found that defects created with the 5 millimeter instrument were inadequate, closing too soon after operation. Those animals surviving the operation in which the 12 millimeter instrument was used, with or without digitalis as an adjunct, died of heart failure within 8 days. Defects created with the 8 millimeter instrument permitted indefinite survival of the animals. Five dogs which were digitalized preoperatively survived defects produced with the 10 millimeter instrument. Four dogs which were not digitalized died within 5 days following creation of defects with the 10 millimeter instrument.

Chronic patent defects. Nine dogs survived for 2 weeks or more with patent defects. Four of these dogs had defects created with the 8 millimeter instrument. Five had defects created with the 10 millimeter instrument and were digitalized for 3 days to 5 weeks depending on the indications for the drug. Each of these groups will be discussed independently.

1. Eight millimeter defects.—In these 4 animals the criteria used for determining the persistence of the defects were the presence of an apical systolic murmur and palpable thrill. The animals recovered quickly from the operation and were observed for these physical signs for 8 months, with 1 exception. This animal died 45 days after the operation of renal insufficiency due to infestation by the kidney worm, Dioctophyme renale. At the time of death the defect was completely healed (Fig. 3). In 2 of the remaining 3 animals the murmurs and thrills disappeared between the third and fourth months after the operation, signifying that the defects healed at this time. These animals were permitted to live 8 months after the operation and then were killed. At necropsy it was found that the defects were healed. In the fourth animal the murmur and thrill persisted until it was killed 8 months after the operation. At necropsy it was found that the septal defect had healed but that a circular piece of the anterior leaflet of the mitral valve had been excised at operation,

TABLE III.—RELATION OF SIZE OF DEFECT AND ASSOCIATED INJURY TO SURVIVAL. PROCEDURES LISTED IN ORDER IN WHICH THEY WERE PERFORMED

Dog	Wt., kgm.	Diameter of instrument, mm.	Results: length of survival, associated injury and cause of death
1	11.2	12	Immediate cardiac failure. Septal tricuspid and aortic leaflets injured
2	12.5		Survived 4 days. Aortic leaflet cut. Aortic insufficiency and cardiac failure
3	11.0		Immediate cardiac failure
4	10.0	10	Survived 30 hours. Heart failure
5	10.1		Survived 5 days. Embolism of left pulmonary artery. Heart failure
6	13.8		Immediate cardiac failure
7	12.5		Survived 18 hours. Heart failure
8	8.2	8	Immediate cardiac failure. Preoperative condition poor. Defect very small
9	12.5		Survived 18 hours. Defect adjacent to right coronary ostium. Coronary artery injury
10	9.0		Survived 2 months, no murmur, thrill observed. Massive pulmonary embolus attached to vegetation at site of healed defect
11	10.5		Ventricular fibrillation occurred during repair of puncture wound of left ventricular wall. Defect very small
12	11.6		Survived. Murmur, thrill not observed. Killed 6 months after operation. Defect healed
13	12.6	8	Immediate cardiac failure. 2 mm. rent in one aortic leaflet
14	10.0		Immediate total heart block. Lived 5½ hours
15	15.6		Survived 11 days. Death probably from paroxysmal ventricular tachycardia. Septal tricuspid leaflet lacerated. Animal very old
16	16.2		Survived. Killed 8 months after operation. Defect healed
17	21.2		Survived. Killed 8 months after operation. Defect healed. Mitral insufficiency caused by excision of portion of anterior mitral leaflet
18	17.0		Survived. Died 45 days after operation of renal insufficiency due to infestation by kidney worm, Dioctophyme renale. Defect healed
19	17.1		Survived. Killed 8 months after operation. Defect healed
20	18.5	10+ digitalis	Survived. Total heart block developed. Died 5 weeks after operation. Defect healed
21	15.5		Survived. Defect healed 1 month after operation. Killed
22	18.5		Survived. Defect healed 2 months after operation. Killed
23	19.0		Survived. Defect healed 1 month after operation. Killed
24	14.0		Survived. Had 4 mm. diameter defect not functioning 1 month after operation. Foramen ovale type of valve created by oblique cut through septum. Killed
25	23.0	12+ digitalis	Died 8 days after operation. Heart failure
26	17.0		Died 12 hours after operation. Heart failure

producing mitral insufficiency (Fig. 4). The hole in the leaflet measured 10 millimeters in diameter and the left ventricle and atrium were enormously dilated. There were "jet" lesions on the endocardial surface of the left atrium. Because this complicating injury also produced a systolic murmur and thrill, it is impossible to say when the defect had healed.

2. Ten millimeters defect plus digitalization.—In these 5 animals, in addition to observation of the physical signs of the defects, cardiac catheterization with the animal under pentobarbital sodium anesthesia was employed as in the acute experiments to demonstrate the presence or absence of an interventricular shunt of blood. These studies were done in each animal 1 month after the operation and 2 months postoperatively if necessary. The defects of 3 dogs were healed at the time of the first cardiac catheterization, also proved by necropsy. One dog had a soft systolic murmur and palpable thrill 1 month after the operation. However, repeated studies by cardiac catheterization failed to show any evidence of a shunt. At necropsy it was found that there was a patent defect 4 millimeters in diameter which passed obliquely through the septum (Fig. 5). As a result, there was a membrane overhanging the left ventricular surface of the defect, created by the injured endocardium of the left ventricular side of the septum. This undoubtedly acted as a valve to close the defect during systole. If any shunt of blood occurred in this dog, it was within the range of error of the methods used to detect it and was therefore not determined. The remaining dog of this series had a patent defect 1 month after the operation through which 31 per cent of the blood entering the left ventricle was shunted into the right ventricle. This defect was healed when the studies were repeated 2 months after operation and this was proved by necropsy.

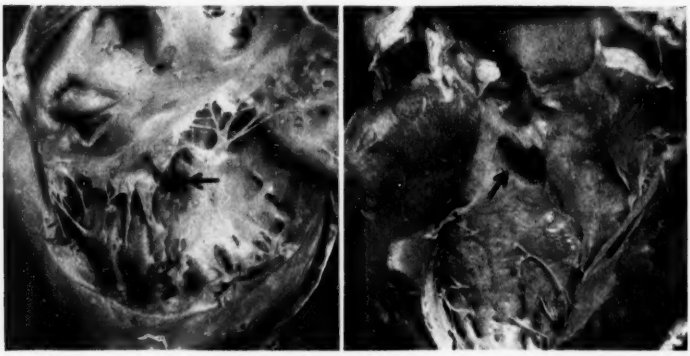
OTHER PHYSIOLOGIC EFFECTS

On creation of the defect there was usually an immediate dilatation of the right ventricle, enlarging to and sometimes beyond the limits of the pericardial cavity. A strong, almost continuous thrill could be palpated, and the contractions of the heart became more vigorous. Tachycardia developed in a matter of minutes and usually persisted for 48 hours, rarely longer than a week if the animal was to survive. In some animals, most often those which died because of excessively large defects, signs and symptoms of heart failure, tachypnea, anorexia, lassitude, pleural effusion and, rarely, peripheral edema developed. If the animal survived, the syndrome of heart failure usually disappeared in 5 to 7 days. From that time until the animal was killed it did not appear to have any limitation of its normal physical capacity.

Fig. 1. The 10 millimeter instrument. a, above, Open. b, Closed.

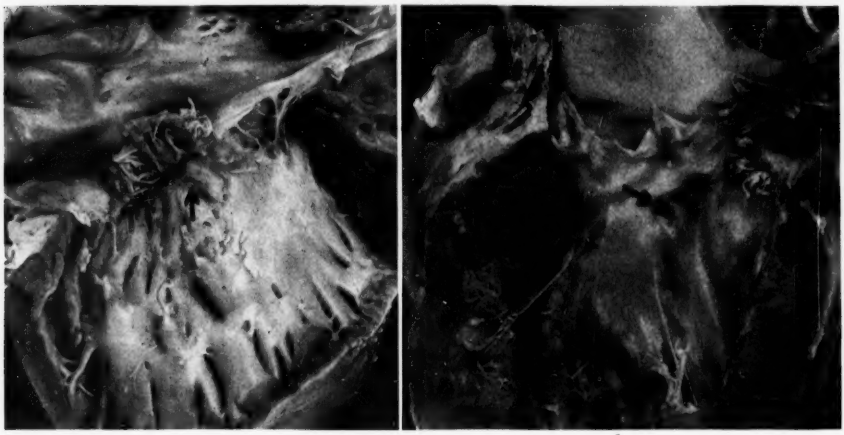
Serial determinations of erythrocyte count and hemoglobin level during the period of patency of the defect failed to reveal any consistent pattern of change. Blood volume determinations in several animals, by the radioactive phosphorus method, showed in 3 to 4 weeks an increase of 15 to 25 per cent in the blood volume. This persisted during the time the defects were patent, with a return to normal after closure of the defects.

Serial electrocardiograms taken one or more times a week after production of the defect revealed some significant changes. Electrocardiographic changes compatible with myocardial damage were minimal and transient, lasting rarely beyond the first postoperative week. The pattern of acute pericarditis, usually making the maximal change between the fourth and eighth postoperative days, was slight as compared with previous reports on pericardial injury (2). Complete or incomplete atrioventricular dissociation and right bundle-branch block occurred, the latter being the more common. In 1 instance a complete atrioventricular dissociation was present with ventricular complexes of the right bundle-branch type. Ventricular extrasystoles were common during the first few postoperative



a b

Fig. 2. Defect produced with 8 millimeter instrument in heart of animal which survived 11 days. a, Right ventricle. b, Left ventricle.



a b

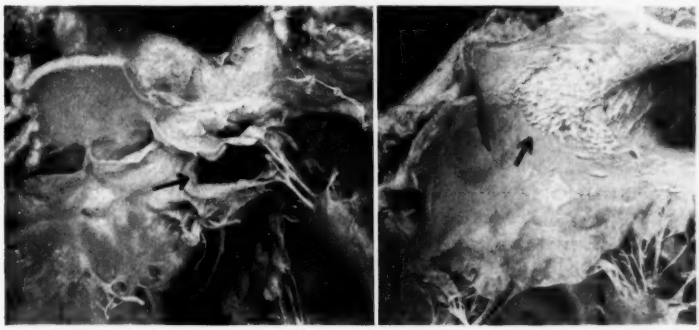
Fig. 3. Completely healed defect created with 8 millimeter instrument. Animal died 45 days after operation. a, Septal tricuspid leaflet reflected upward showing scar. b, Scar seen beneath aortic valve.

days; these extrasystoles frequently occurred in short runs, constituting a ventricular tachycardia.

In 1 animal with general cardiac enlargement believed due to an associated mitral insufficiency, a right bundle-branch block developed immediately after operation and persisted until the fifty-second day after the operation, when the electrocardiogram again returned to normal range. Occasional transient changes consisting of increased potential of the *R* wave were seen in the 1 dog with cardiac enlargement. Such changes were consistent with ventricular enlargement.

PATHOLOGIC FEATURES

There was formation of mural thrombi on the wound edges of the septal defect with necrosis and cellular infiltration of the underlying muscle as early as 5 hours after operation. Within 18 hours after operation, early organization of the thrombi was seen. In 2 instances the septal branch of the left coronary artery was probably injured. When the dogs died 5 days and 11 days, respectively, after the defects were created, infarction of the septum around the defect was evident on microscopic examination. Organizing throm-



a b

Fig. 4. a, Hole in anterior mitral leaflet inadvertently created during production of septal defect. b, "Jet" lesions on endocardial surface of the left atrium.

a b

Fig. 5. Unusual result of healing 1 month after operation of defect created with 10 millimeter instrument. a, Right ventricular aspect. b, Left ventricular side showing endocardial membrane overhanging the defect.

bus formation was present in these specimens over the necrotic muscle. Healing of the defects proceeded with dense scar formation, the result of organization of mural thrombi on both sides of the defects, in which were seen blood vessels with thick muscular walls and narrow lumina. Foci of fibrocartilage were found in every healed defect. There were sheets of cells in the scars, resembling smooth muscle, extending from one ventricular surface of the septum to the other. In the animal with mitral insufficiency, the defect just beneath the aortic valve was completely healed. "Jet" lesions in the left atrium were focal areas of thickening of the endocardium which consisted of collagen, containing elastic tissue and smooth muscle cells. In this dog hypertrophy of the left ventricle was grossly apparent. While dilatation of the right ventricle was seen in most animals before healing of the defects, no gross or microscopic evidence of right or left ventricular hypertrophy was found in any other dog.

COMMENT

It was not anticipated in view of the work previously done in this field that the interventricular septal defects would heal. Instead, it was hoped that an experimental method of producing defects which would remain patent indefinitely could be standardized for future experimental use. Why our results differ from those of earlier workers remains to be explained. In spite of the continual passage of

great quantities of blood under pressure through the fenestrations, the defects uniformly healed.

It is speculative whether the knife of Holman and Beck created narrow elliptical fenestrations which were initially longer though not as wide as those which we produced and which gradually dilated to form circular defects of diameters comparable to those created by us. This period of gradual dilatation would permit the adaptation of the heart to its altered functions. The longer initial character of the hole would perhaps resist more successfully the influence of healing than did the circumscribed defect used in our experiments.

Of the dogs that survived, all the defects created were in the muscular portion of the interventricular septum. Were it possible to produce them in the membranous portion of the septum the likelihood of their healing might be less. Interatrial septal defects in dogs are created in relatively thin tissue and they rarely heal (1, 10). Efforts were made by us in many dogs during unreported acute experiments to produce a defect in the membranous portion of the interventricular septum. However, the membranous portion of the interventricular septum is too small and too close to the tricuspid and aortic valves to permit consistent success in a blind procedure.

SUMMARY AND CONCLUSIONS

An experimental method and an instrument have been developed by which interventricular septal defects of a known initial size can be created in dogs. Average quantities of blood passing through such defects in the early period of their existence were 41 to 83 per cent of the blood entering the left ventricle. It was found that the defects which permitted indefinite survival ranged initially from 8 to 10 millimeters in diameter. However, it was found that such defects healed in every instance in from 1 to 4 months.

Electrocardiograms, erythrocyte counts, hemoglobin and blood volume determinations were made preoperatively and at intervals after creation of the defects. Significant changes in the erythrocyte counts and hemoglobin levels were not noted. An elevation of the blood volume of 15 to 25 per cent was observed during the period of patency of the defects. Complete or incomplete atrioventricular dissociation and right bundle-branch block were frequently seen in the postoperative electrocardiographic tracings. Histologic examinations revealed the formation and organization of mural thrombi on the wound edges of the septal defect, with eventual dense scar formation in which were found sheets of cells resembling smooth muscle and many foci of fibrocartilage.

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THE DIAGNOSIS AND TREATMENT OF ECTOPIC PREGNANCY

An Analysis of One Hundred Forty Recent Cases

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THE frequency of ectopic pregnancy is increasing annually in the United States. Concurrently the mortality incident to this disease is decreasing at approximately the same rate. There is a direct relation between live births and the occurrence of ectopic pregnancy. Between 1936 and 1948 there was an increase in the birth rate in this country of 64.8 per cent. The occurrence of ectopic pregnancy paralleled this increase in birth rate.

The analysis of 140 cases of ectopic pregnancy surgically treated in the Jefferson-Hillman Hospital over a 5 year period, July 1, 1945 to July 1, 1950, forms the basis of this study. Seventy-seven cases were treated on the charity gynecological service, and 63 cases were treated on the private gynecological and surgical services. During this 5 year period 144 cases of ectopic gestation were treated. Four of these cases were beyond the twenty-eighth week and were tabulated as advanced abdominal pregnancy, 3 of which have been reported previously (3).

Frequency. The number of ectopic pregnancies occurring annually in the United States has been calculated to be in excess of 21,000. During the 5 year period mentioned ectopic pregnancy occurred 59 times in the white race and 85 times in the colored race. Simultaneously in the same institution there were 8,295 live births in the white maternity and 8,141 live births in the colored maternity, which gives a ratio of 1: 140.6 in the white and 1: 95.8 in the colored race. The percentage of hospital deliveries in Jefferson County (Birmingham), Alabama, closely parallels the percentage in each race over the country as a whole. In 1948 there were 2,784,865 hospital white live births in the United States and 240,341 hospital colored live births.

$$\frac{2{,}784{,}865}{140.6} \text{ plus } \frac{240{,}341}{95.8} \text{ equals } 22{,}310$$

In Baltimore, Maryland, Anderson found that ectopic pregnancy occurred in the ratio of 1: 177 total live births in the white race and 1: 121 total live births in the colored race. In 1948 there were 3,080,316 total white live births in the United States and 454,752 total colored live births.

$$\frac{3{,}080{,}316}{177} \text{ plus } \frac{454{,}752}{121} \text{ equals } 21{,}161$$

These two groups of figures closely parallel each other and are more than coincidental. It is believed the frequency of ectopic pregnancy calculated on the basis of live births is more accurate than when the estimation is based on total pregnancies. Abortions can only be estimated; many are never recorded.

Etiology. Nothing new in this study was encountered to explain the etiology of this disease in all cases; however, 33.5 per cent of the tubes submitted to the laboratory showed microscopic evidence of salpingitis.

Race and age. Of the 140 cases of early ectopic pregnancy analyzed in this report, 59 cases occurred in the white race and 81 cases occurred in the colored race. The age distribution is shown in Table I.

TABLE I.—AGE DISTRIBUTION

Age, years	No. patients
Under 20	5
20 to 30	67
30 to 40	66
Over 40	2

Mortality. Thirteen years ago Von Graff and Brown estimated the mortality for ectopic pregnancy to be 5 or 10 per cent. Since that

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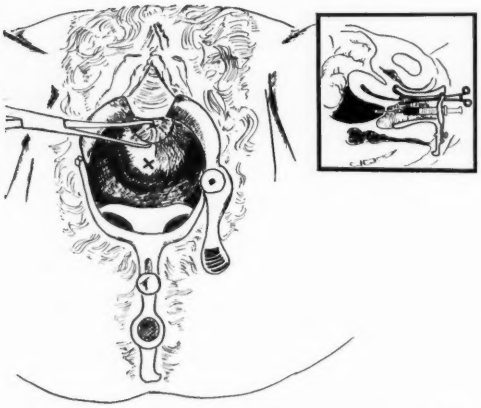

Fig. 1. The technique of cul-de-sac aspiration. *X* designates where 18 gauge needle should be inserted.

time there has been a steady decrease in the mortality of this disease. From 1936 to 1948 there was a 50 per cent reduction in annual deaths. This occurred despite a 64.8 per cent increase in birth rate or a reduction in mortality of 69.7 per cent as shown in Table II.

Beacham and associates quote a 2.89 per cent mortality for the cases treated at Charity Hospital over a 10 year period ending in 1946. The current mortality of this disease for the entire country, based on the average annual deaths from 1944 through 1948 and using 21,000 cases as the number that occurs annually in the United States, would be approximately 1½ per cent. This dramatic reduction in mortality is due to the free use of blood from the blood banks that have been established throughout the country since 1940. Earlier correct diagnosis, improved surgical technique, and the antibiotics have played an important part in this reduction; however, the immediate availability and use of blood has been of greatest value. If correct early diagnosis is made and proper treatment instituted the mortality rate of this disease should approach zero. Even in cases of advanced abdominal pregnancy a history of tubal rupture in the early period of gestation can be obtained.

TABLE II.—MORTALITY FROM ECTOPIC GESTATION IN THE UNITED STATES (4)

Year	Number of deaths from ectopic gestation	Live births	Rate per 100,000 live births
1936	486	2,144,790	22.65
1937	461	2,203,337	20.92
1938	437	2,286,962	19.10
1939	374	2,265,588	16.51
1940	392	2,360,399	16.61
1941	358	2,513,427	14.24
1942	346	2,808,996	12.32
1943	332	2,934,860	11.31
1944	345	2,794,800	12.34
1945	334	2,735,456	12.21
1946	329	3,288,672	10.00
1947	300	3,699,940	8.11
1948	243	3,535,068	6.87
Per cent decrease	50.0	64.8 (increase)	69.7

SYMPTOMS

Pain. It is imperative that early correct diagnosis be made in this disease for a continued reduction in mortality. The intelligent interpretation of the symptoms, signs, and laboratory aids are the only means at hand in making such a diagnosis. Of the symptoms, signs, and laboratory studies recorded on the charts of 140 ectopic pregnancies, abdominal pain was the most constant finding recorded. Ninety-seven and eight-tenths per cent of all patients complained of abdominal pain; 3 patients did not complain of this symptom. All 3 had unruptured tubal pregnancies. The pain, most often, was sudden in onset. The patient remembered exactly what she was doing at the time. Four patients stated the onset of their pain occurred during intercourse. Often the pain would subside and in a few days recur more severe than ever. Many patients had exaggeration of pain at stool or urination. Fifteen and seven-tenths per cent of the patients experienced pain in the shoulder and 5 per cent in the epigastrium.

Vaginal bleeding. Vaginal bleeding occurred in 127 patients (90.7 per cent). Of 13 cases with no vaginal bleeding, 10 were ruptured, 2 were unruptured, and 1 was a 10 month old dead tubal pregnancy in a patient with a 4 month intrauterine pregnancy. The bleeding usually had its onset 2 weeks after a missed period and was characterized by the passage

of dark blood or "spotting"; however, a few patients bled rather profusely per vagina.

Amenorrhea. Amenorrhea occurred in 88 patients (62.8 per cent). Very often the patient who is late a few days starts bleeding and assumes the bleeding to be a regular normal menstrual period. If her physician is not alert he, too, may believe the bleeding to be physiological. Unless he considers ectopic pregnancy in the differential diagnosis in any female patient between the ages of 14 and 44 who complains of abdominal pain, a history of amenorrhea is likely to be improperly recorded. To obtain a correct menstrual history one must constantly bear in mind the possibility of ectopic pregnancy; otherwise, a slight deviation from the normal menstrual cycle is apt to be dismissed with the following notation: "Periods regular and normal; began 14x30x4."

Other symptoms noted were fainting, nausea and vomiting, thirst, dysuria, and an urge to defecate but inability to do so. Their importance must be evaluated, together with the symptoms already recorded.

SIGNS

Abdominal tenderness was the most constant sign recorded. It was present in 130 of the patients (92.8 per cent). This tenderness, often generalized, was usually more pronounced on the affected side.

The next most common sign was a tender cervix detected on vaginal examination. This sign was positive in 84 patients.

A pelvic mass detected on bimanual examination was the third most common sign. It was recorded in 80 cases (57.1 per cent).

The next most common sign was a soft cervix. The cervix felt like an intrauterine pregnancy in 69 patients.

The uterus was recorded as enlarged in 49 patients. In tubal pregnancy the uterus enlarges during the first 6 to 8 weeks at the same rate as it would if the pregnancy were intrauterine.

Seventeen and one-tenth per cent of the patients were admitted to the hospital in a state of shock. One patient went into shock in the ward after 5 examinations and another after 1 examination. Air hunger was a common sign found in the patients in or approaching shock.

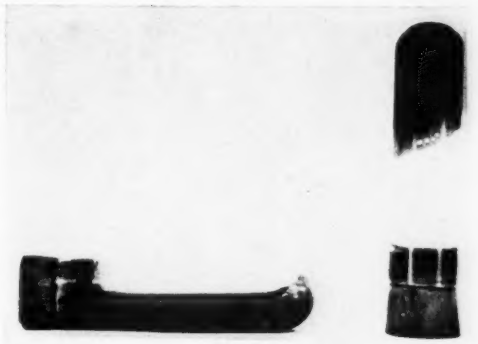

Fig. 2. The horizontal tube contains blood from the cul-de-sac and is not clotted. The vertical tube contains venous blood and is clotted.

The temperature in this series ranged from 96.6 to 101.2 degrees F. In most instances it was 99 to 100 degrees F. When it rises above 101 degrees F. some complication should be suspected or another disease considered.

DIAGNOSTIC PROCEDURES AND LABORATORY AIDS

Cul-de-sac aspiration. The most consistently positive diagnostic test was the cul-de-sac puncture. This was done in 53 cases and was positive in 51 (96.8 per cent). In the 2 negative punctures in which pregnancy was present in the tube, one was unruptured, and in the other case 150 cubic centimeters of fresh blood was found in the cul-de-sac. This blood may have accumulated following rupture, incident to examination after cul-de-sac puncture. There were 3 positive cul-de-sac punctures in which exploratory laparotomy proved no ectopic pregnancy was present. In 1 case no blood was found in the peritoneal cavity, only a hematoma on the anterior rectal wall. In the second case bilateral chronic salpingitis was present and an old hematoma found in the cul-de-sac. The third positive puncture was due to rupture of a corpus luteum cyst with 500 cubic centimeters of blood found in the peritoneal cavity. If we add these 3 false positive tests and the 2 false negative cul-de-sac punctures we still have a diagnostic test that is 90 per cent correct.

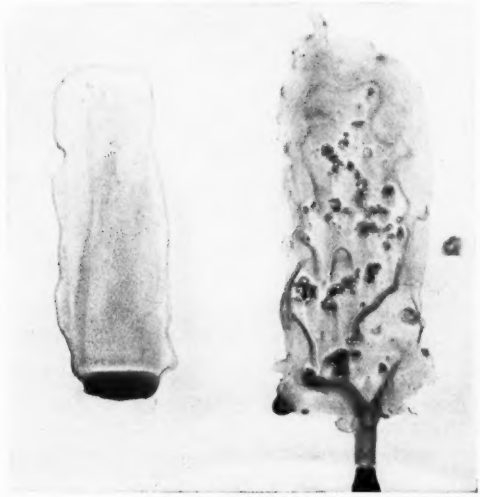

Fig. 3. Blood smear on the left is a drop of venous blood. It smears homogeneously. Blood smear on the right is from cul-de-sac and demonstrates small dark flakes of fibrin.

There is no diagnostic laboratory test for ectopic pregnancy that has been proved correct in as high a percentage of instances. We feel that this test is simple and harmless and only slightly more difficult than drawing blood from the vein of an extremity. Our residents perform this test in the emergency room on any patient suspected of harboring a ruptured ectopic pregnancy. In 5 years of extensive employment of cul-de-sac aspiration by our house staff there has been no sequela. The possibility of withdrawing blood from a pelvic vein instead of the cul-de-sac and thereby being misled by the test is the foremost criticism of this procedure. Blood from a pelvic vein will clot in 10 minutes, but blood from the cul-de-sac will not. Extravasated blood in the peritoneal cavity from a ruptured ectopic pregnancy clots. This clot is agitated by motion of the patient and the intestinal tract. The peritoneum reacts by expressing a transudate that mixes with the serum, red blood cells, and fibrin flakes from the clot. The bloody mixture withdrawn by needle puncture may be indistinguishable from venous blood in gross appearance, but if ejected on a white cloth or glass slide small dark flakes of fibrin will be noted. Laparotomy revealed blood in the peritoneal cavity in 127 of the 140 cases. In 19 cases rupture had not occurred although in 6 of these extravasated blood was present and a positive cul-de-sac puncture would have been secured. By this simple test, if done in all cases, correct diagnosis would have been facilitated in 90.7 per cent of the cases. Cul-de-sac puncture, like any other diagnostic aid, is subject to intelligent interpretation. Occasionally a tubal pregnancy is ruptured by an overzealous examiner. Immediate cul-de-sac aspiration in such cases would yield fresh blood.

Blood picture. The total red blood cell count is the most important part of the blood picture. It is usually reduced in intra-abdominal hemorrhage and was as low as 1¼ million in 2 of our cases. The hemoglobin parallels the red cell count. Often the red cell count is much lower a few hours after rupture because of the hemoconcentration immediately following hemorrhage. Anemia alone is not a cause of shock in intra-abdominal hemorrhage, as some of the patients in this series walked into the hospital with a red cell count of 1½ million while others were in shock with a red cell count of 3½ million. Ruptured ectopic pregnancy should be suspected in any female patient in the child-bearing age who complains of abdominal pain and has an anemia out of proportion to external blood loss.

Sedimentation rate. The sedimentation rate may be helpful in differentiating acute salpingitis from ectopic pregnancy; however, we found it of little actual value in this series.

Hormonal pregnancy test. The hormonal pregnancy test was found to be positive in 11 cases. Two false positives were recorded and 2 false negatives. A positive Friedman test is indicative of living chorionic villi some place in the reproductive tract and is of no help in differentiating between an intrauterine and extrauterine pregnancy. The majority of the cases in this series had symptoms of rupture for more than 5 days. In patients with symptoms of rupture of several days' duration the chorionic villi that remain are nonfunctioning, or the hormone they produce is insufficient to cause a positive Friedman reaction.

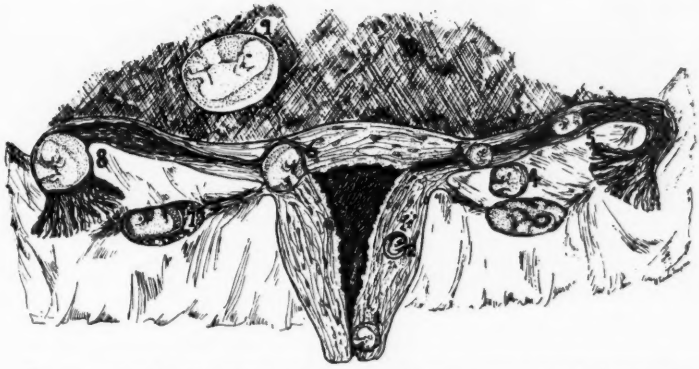

Fig. 4. Various locations where ectopic pregnancy may occur: *1*, cervical pregnancy; *2*, pregnancy in adenomyosis of uterine wall; *3*, pregnancy in isthmus of tube; *4*, intraligamentous pregnancy; *5*, pregnancy in ampullary portion of tube; *6*, interstitial pregnancy; *7*, ovarian pregnancy; *8*, pregnancy aborting from fimbriated end of the tube; *9*, abdominal pregnancy.

Dilatation and curettage. This procedure was recorded as having been done 9 times. Positive decidual reaction was found on microscopic examination only 3 times. If bleeding has been present for more than a week most of the decidua has shed. In 2 instances the diagnosis was made on preoperative examination by finding a decidual cast in the vagina. One was removed from the cervix by the writer with a sponge forceps and was helpful in making the diagnosis. The structure was thin and ribbon-like and gave the appearance of a discarded snake skin. Four patients passed decidual cast postoperatively. A dilatation and curettage is helpful in differentiating an intrauterine pregnancy. If only decidual reaction is found in the intrauterine scrapings it is suggestive of ectopic pregnancy but not confirmatory, as corpus luteum cysts may produce a decidua-like change, as well as a positive Friedman test.

LOCATION OF LESION

The lesion was found 85 times in the right tube, 54 times in the left tube, and once in the right ovary. The location of the pregnancy in the tube was noted to be 1 time in the interstitial portion, 9 times in the isthmus, and 127 times in the ampullary and fimbriated end of the tube. One pregnancy was found in the cul-de-sac and 1 between the leaves of the right broad ligament; however, in each of the last 2 instances a damaged tube from which the fetus escaped was removed.

PREOPERATIVE DIAGNOSIS

Of the 140 cases of ectopic pregnancy the preoperative diagnosis was made correctly in 122 patients (87.1 per cent). Sixteen patients, during the same 5 year period, were operated on for ectopic pregnancy and the pregnancy not found. In the entire series mistakes in preoperative diagnosis were made in 34 instances or a corrected diagnosis of 75.7 per cent. The incorrect preoperative diagnosis in the 34 cases is listed in Table III.

One patient did have a myoma. The ectopic pregnancy was an incidental finding, as was true in the case of carcinoma in situ. One patient had a ruptured corpus luteum cyst and 500 cubic centimeters of blood was found in the cul-de-sac. The patient with the hematoma of the right tube had 200 cubic centimeters of old blood in the cul-de-sac. This may have been a case of ectopic pregnancy. Since no tissue was removed and no surgery other than exploration was done, we have no proof that the condition was an ectopic pregnancy and are therefore listing it as a missed diagnosis.

It can readily be seen from Table III that 11 missed diagnoses were due to ovarian cysts and 12 were due to infections of the pelvic organs.

TABLE III.—INCORRECT PREOPERATIVE DIAGNOSIS

Preoperative diagnosis as listed (Proved to be ectopic)	No. cases	Preoperative diagnosis ectopic pregnancy (Proved to be as listed)	No. cases
Uterine myoma	4	Salpingitis	6
Ovarian cyst	4	Follicle cyst	3
Tubo-ovarian abscess	4	Corpus luteum cyst	3
Appendiceal abscess	1	Mittelschmerz	1
Appendicitis	1	Tuberculous peritonitis	1
Pyosalpinx	1	Exploration—no disease found	1
Carcinoma in situ of the cervix	1	Hematoma of right tube	1
Intestinal obstruction	1		
Endometriosis	1		
Total	18	Total	16

A careful history, a thorough physical examination, and the employment of all helpful diagnostic procedures are mandatory in making a correct preoperative diagnosis in all but the typical case.

TREATMENT

The main features of the treatment of this disease are replacement of blood loss and control of the hemorrhage. This is accomplished by immediate, persistent whole blood transfusions, sufficient to restore the blood picture to normal, and immediate laparotomy with total excision of the ruptured tube. Most authorities feel that immediate operation is necessary and should be performed as soon as blood is available to start simultaneously. However, with modern blood facilities blood can usually be run into a patient faster than it can leak out of the ruptured sight, even if several ports of entry are necessary. In this series 1 death occurred which was partially due to mismanagement, that is, operation before replacement of blood loss. The great majority of patients enter the hospital after having bled for several hours or days. These patients will do much better if they receive replacement of blood while preparations for laparotomy are being made. This point is borne out in a case that was reviewed in this series. The patient was taken to the operating room with a presumed diagnosis of appendiceal abscess. A McBurney incision was made, and the abdomen was found to be full of blood. Because of the patient's severe anemia, less than 2 million red blood corpuscles, the surgeon closed the incision, typed the patient for blood, gave several blood transfusions and operated on the patient 2 days later. Her convalescence was uneventful. In this group of patients a total of 136,000 cubic centimeters of blood was given, an average of 971 cubic centimeters per patient. Five patients received no blood. One patient received 4,000 cubic centimeters of blood. In every case the patient received adequate amounts of blood. The patient who died received an adequate amount but it was given at the wrong time, after instead of before operation.

Total salpingectomy is the procedure of choice in the surgical treatment of this disease; hysterectomy may be necessary in the interstitial type. It has been oft repeated "control the hemorrhage and get out." The latter can usually be done by placing a clamp on each side of the ruptured area, excising the injured portion of the tube and ligating the tissue between clamps. This adequately controls the hemorrhage but leaves a stump adjacent to the uterus in which future pregnancies may occur. Two such instances were recorded in our experience. In one instance the ovary had been removed from the opposite side, and presumably the ovum in this case externally migrated to the opposite tube, came back through the uterus, and implanted itself in the tubal stump. Usually excision of the entire tube is no more difficult than excision of the injured portion of the tube. If no more children are desired and the stump of a tube is left, the opposite tube should be ligated. In cases of massive intraperitoneal hemorrhage, excision of the affected tube is all that should be done. In cases of an unruptured ectopic or minimal hemorrhage other indicated surgery may be performed, depending upon the condition of the patient and good judgment and skill of the surgeon. In this series removal of the fetus was done in 1 instance, in 20 cases salpingo-oophorectomy, in 8 salpingectomy and appendectomy, in 88 salpingectomy, in 3 subtotal hysterectomy (1 interstitial pregnancy), in 1 "double ligation of rupture," in 1 removal of fetus and placenta, in 1 oophorectomy, and in 7 partial removal of tube. One hundred thirty-nine of these cases were treated surgically through the abdomen. In 1 case

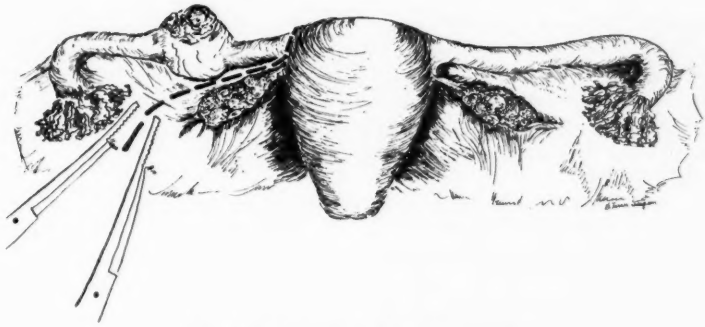

Fig. 5. Technique of total salpingectomy.

the tube was removed through the posterior vaginal fornix. In 2 other cases removal was attempted through the vagina but could not be successfully accomplished by this approach. In 1 instance the omentum was wrapped around the tube and could not be freed. In the other case the tube could not be delivered into the vagina, and massive hemorrhage into the peritoneal cavity obstructed vision. Both were treated successfully by laparotomy.

In cases of rupture the peritoneal cavity is filled with varying amounts of blood. When the peritoneum is opened the operation will be facilitated by grasping the uterus with a uterine elevator and lifting it into view. In this manner both tubes and ovaries can be inspected and the pregnancy quickly located. After the necessary surgery has been done, clots should be removed from the peritoneal cavity. Autotransfusion was not done in any of our patients. It may be a lifesaving measure when blood is not available from any other source.

COMPLICATIONS

The complications were few in this series. There was only 1 of serious proportion and that was thrombophlebitis of the left femoral vein. There were 2 pelvic abscesses that required drainage through the cul-de-sac and 4 wound infections, 3 of which were very slight.

REPORT OF DEATH

The death we feel in retrospect was preventable, although Williams and Corbit considered a death nonpreventable if immediate surgery was done as soon as diagnosis was made, and blood was given in adequate amounts during and after operation.

The patient was a 26 year old colored female admitted as a private patient September 26, 1949. Her illness began September 4, 1949, three weeks prior to admission, when she experienced sudden abdominal pain and fainted. Her last menstrual period was June 15, 1949. Shortly after the onset of abdominal pain, vaginal bleeding developed and continued to the time of admission. The patient was treated by her private physician with penicillin for septic abortion for 5 days. On September 30, the patient was transferred to the charity gynecological service, at which time she had a red blood cell count of 1,540,000. One 500 cubic centimeter blood transfusion was given. On October 2, the patient's seventh hospital day, a cul-de-sac puncture was done, and at this time the diagnosis first became apparent. The patient was taken to the operating room at 11:30 a.m. with a hemoglobin of 21 per cent, pulse of 120, and a blood pressure of 136/80. A transfusion was started in the operating room, and a laparotomy was performed. A ruptured ectopic pregnancy of the left tube was found. The patient received 3,000 cubic centimeters of blood during and immediately following the operation. The blood pressure at the end of the operation was 70/36 and pulse 160. The patient remained in shock following the operation and died at 4:20 p.m. An autopsy revealed the cause of death to be irreversible postoperative shock.

This death was due to delay in making a correct diagnosis during the 7 days of hospitalization and failure to replace blood loss before operation.

SUMMARY

The symptomatology, signs, and certain diagnostic tests recorded on the clinical records of 140 ectopic pregnancies studied during a 5 year period in one hospital have been reviewed. The 4 most constant characteristics

of ectopic gestation as found from this analysis are: abdominal pain, abdominal tenderness, vaginal bleeding, and the finding by needle puncture of blood in the cul-de-sac.

No single symptom or sign is indicative of ectopic pregnancy, but if each sign or symptom is evaluated carefully and the indicated diagnostic test done immediately, fewer mistakes in diagnosis will be made.

The proper treatment for ectopic pregnancy is immediate replacement of blood loss by whole blood transfusion and total extirpation of the affected tube.

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SACROCOCCYGEAL TERATOMAS IN INFANTS AND CHILDREN

A Report of 40 Cases

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OF the more important teratomas in infants and children, those appearing in the sacrococcygeal area are the most common. During the 30 year period ending May 1, 1950, forty such cases have been studied in the Children's Hospital of Boston by various members of its surgical staff, 28 of these having appeared for treatment in the last 10 years. Thirty-three of the group have been traced for more than 3 years, and 37 of them for more than 2 years; this rather complete follow-up permits us to give a reasonably accurate evaluation of the long term results of therapy. A description of the clinical problem, the pathologic characteristics, and the surgical management of these cases is the basis of this report.

The earliest record of a teratomatous malformation in the sacrococcygeal area was made on a Babylonian cuneiform tablet in Chaldea about 2000 B.C. According to legend, this child was born with a posterior appendage projecting from the sacral area and was looked upon as a favorable omen, because "when a woman gives birth to an infant that has three feet, two in their normal position, and a third between them, there will be great prosperity in the land" (2). Apparently the Chaldeans were more interested in forecasts than they were in a deformed individual.

These lesions are found largely in infancy or early life. They are much more common in females. Calbet, a half century ago, despairing of finding an adequate explanation for this sex predominance, recalled Aristotle's statement that "the first mistake of nature was in creating a female."

The first successful surgical extirpation of a sacral teratoma was reported by Blizard (14) in 1841. Since that time there have been numerous reports of individual cases or small series which, in general, have lacked sufficiently complete follow-up studies to permit accurate computation of malignancy, mortality rates, and recurrence expectancy. Though several authors in recent years have given the impression that less than 100 cases have appeared in the literature, we have been able to collect 426 from infants and children.

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PATHOLOGY

We have been fortunate in having the valuable aid of Dr. Sidney Farber in whose Department of Pathology all of our specimens have been examined.

Sacrococcygeal teratomas have been found in widely varying ages, but the vast majority are lesions of early life. They have been described in a 3 months old fetus (1). They are most commonly observed at birth or shortly thereafter. A few have been found in older children. Only rarely do they appear in adults.

Teratomas are composite masses possessing more than one germinal layer. Wherever adequate examination was possible, tissues representing all three germinal layers were found in each of our specimens. A wide range of tissue maturation may be found from case to case, and indeed in different portions of one specimen. Some tumors are composed almost entirely of cells from a single germinal layer; careful search is required to demonstrate the other cell components and recognize the teratomatous nature of the mass. Attempts to classify sacrococcygeal growths as "dermoids," "teratoids," "included twins," and "fetal parasites" should be avoided; it is better to group all of them together under one general term of "sacrococcygeal teratoma."

We have placed in this category all of those tumors arising in the region of the coccyx which possess derivatives from more than one germ layer.

Sacrococcygeal teratomas may pursue one of two courses. They may persist as benign, well encapsulated, cystic or solid affairs that grow at about the same rate as the host and are symptomatic only by virtue of size or by displacement of adjacent organs. Conversely, one element may at any time discard its mantle of benignancy and burst forth as a rapidly growing tumor which invades nearby structures, enters lymphatics and blood vessels, metastasizes widely to nodes, lung, or skeleton, and leads to death of the child within a few months. Many of the lesions which pursue the latter course arise from exceedingly small and presumably quiescent tumors. In a few instances, surgical meddling or incomplete removal of an apparently innocuous lesion seems to stimulate it into a hopeless malignancy. In our 40 cases, there have been 11 which exhibited histologically malignant characteristics; 7 of these had at one time or another local invasion into the sacrum, et cetera, or had metastases to lymph nodes (inguinal or retroperitoneal), liver, lungs, or distant bones.

These growths present a wide variety of gross appearances. They are smooth or irregularly shaped. They range from tiny lesions a few centimeters in diameter to huge ones which may be much larger than the baby's head. Often they have been so large that they interfered with delivery of the child. They may be completely solid, largely cystic, or any combination of the two. They are covered by skin which may be tense and shiny, or may be wrinkled and rough; in most instances, they are devoid of hair. They are situated in the sacral area or buttocks, whence they tend to grow posteroinferiorly to form a large protrusion over the sacral and perineal regions. Many of them have a propensity to dissect anterosuperiorly into the hollow of the sacrum and thereby displace and greatly distort regional organs or tissues such as the rectum, vagina, buttocks, et cetera, without actually invading them. This is a point of practical interest, because even the largest masses can usually be shelled out without destruction or removal of adjacent viscera. An extension of this sort may reach up into the retroperitoneal areas. Rarely (in 2 of our cases) the tumor entered the spinal canal and grew upward extradurally as a finger-like projection. It is very important to recognize that these teratomas almost always have an attachment to the coccyx or even to the lowermost part of the sacrum; obviously, it is necessary in all cases to remove the entire coccyx when striving for a complete eradication of the neoplasm.

In general, those masses which are largely cystic are more apt to be relatively benign when examined microscopically, but such a relationship is not always found. While an entirely solid mass might arouse fears of malignancy (which indeed might be present), histologic study often reveals only well differentiated tissues.

A very large lesion does not necessarily imply a poor outlook. Some of our most gratifying results have come in babies who had enormous tumors; conversely, some of the smallest lesions proved to be the most unsatisfactory as far as curability was concerned.

Cut surfaces of these teratomas show great variations in structure. Some are largely cystic, others are entirely solid; the two forms are commonly intermingled in an irregular way. Some specimens contain hair or sebaceous material; others have fluid which is clear yellow, or is cloudy. Only 2 of our specimens showed appendages or grossly recognizable organs (a rudimentary face, and a well developed tooth), but such have been described in 10 to 15 per cent of those in the literature. The solid areas may be scirrhous, or may be soft and highly cellular. Irregular calcification appears in many specimens, but this should not be regarded as an indication that the entire structure is well differentiated and benign.

By microscopic examination, representatives from each germ layer have been found. All types of tissues have been encountered excepting cardiac musculature, placental tissue, and gonads (though testes and ovary have been described in several of the reports in the literature). Skin, alimentary tract

lining, salivary and pancreatic glands, respiratory tract structures, portions of metanephros, cartilaginous and osseous formations, smooth and striated muscle, and nerve tissues are commonly seen in benign lesions. Of the malignant teratomas, 4 have been classified as embryoma, 4 as papillary adenocarcinoma, 1 as a rhabdomyosarcoma, and 2 as malignant neural tissue or neuroblastoma. When the neoplasms were predominantly neural (ependyma, choroid plexus, nerve fibrils, gray matter, neuroblastoma, et cetera), the subsequent incidence of recurrence was strikingly high (4 times that of the other more pleomorphic specimens).

THEORIES OF ORIGIN

We, with others, believe that teratomas arise from primordial cells which may be pluripotent (capable of producing at least two germ layers) or totipotent (capable of producing cells representing all three germ layers). One would expect teratoma formation to occur more frequently in those locations where the greatest concentration of primitive cells exists in a fetus over the longest period of time. Such areas would include (1) the area of the "primitive knot" and (2) that of the reproductive gland anlage.

The great frequency of appearance of teratomas near the coccyx is readily explicable. It is here that the "primitive knot" (Henson's node) is finally located and its totipotent cells are apt to split off and give rise to neoplasms. In the midportion of the fetus are the unsegmented mesoderm, the neural canal, and the developing somites (Fig. 6). As the somites and neural tube develop cephalad, there is a caudal migration of the primitive knot (Henson's node) so that this focus is literally pushed far out onto the tip of the developing tail. During subsequent embryonic development, the tail in the human undergoes resorption and progressive fragmentation so that there is a gradual condensation and contraction until its final form is achieved. During this process of dissolution and shortening of the tail, the remnant of the primitive knot comes back to rest in the region of the coccyx. This hypothesis proposed by Calbet, Brindley, and others, and more recently amplified by Dr. F. L. Bremer, consulting embryologist to the Children's Hospital, has many attractive features; it nicely correlates known embryologic events to the known high concentration of teratomas in the coccygeal area.

The primitive knot is the nidus from which the fetus develops. Among the many structures which arise from it are the "genital" cells, these being given off by it as the knot shifts toward the lower end of the body as previously described. These genital cells migrate anteriorly and become concentrated in the developing urogenital ridge. The cephalad portion of this ridge develops first, but it atrophies early at 14 to 24 days of age. However, the caudal portion of the ridge persists, becomes thickened, and forms an undifferentiated reproductive gland at 27 to 35 days of age. The longer persistence of the caudal portion of the ridge gives a higher chance for regional splitting off of cells and formation of teratomas in the abdomen and pelvis, rather than in the thorax. In a male embryo, the reproductive gland anlage differentiates abruptly at 31 to 34 days of age, and forms a testis. However, if an embryo is destined to become a female, no definite changes may occur in the reproductive anlarge until 39 to 50 days of age, when the ovary slowly begins to develop. Obviously, genital cells have a shorter time to become ectopic during the brief development of the testis of the male embryo, while in the female the process of ovarian formation is prolonged by at least 5 to 15 days and there is an increased chance for aberrations to occur. We believe that this mechanism might possibly account for the higher incidence of sacrococcygeal teratomas in the female.

In short, it would seem that primitive cells could: (1) come directly from a primitive knot and give rise to those neoplasms which are contiguous to the coccyx, or (2) traverse through the reproductive gland anlage and give rise to those teratomas which develop in front of the sacrum.

CLINICAL DATA

Thirty-two of the 40 patients were females, a marked predominance also noted by others.

Other congenital anomalies of serious importance were rare. One infant had an anomalous development of the thoracic spine. One had an incomplete cleft of the soft palate. The routine histories, taken at the time of hospitalization of our patients, revealed only rare malformations in the families of these youngsters.

Questionnaires have been sent recently to the families of all patients and the incidence of twinning in blood relatives (parents, grandparents, uncles and aunts, or first cousins) has been sought. From the 40 questionnaires, 23 replies were received. In 3 cases the patient was one of twins; in at least 1 of these instances the twins were identical. In addition to these 3, 8 of the 23 families have had twin births, and 1 has had triplets. Therefore, the occurrence of twinning in our series was at least 12 out of 23, or more than 50 per cent. This is significantly higher than that normally expected in the general population.

For reasons of prognosis, it is important to place in separate categories those teratomas which are noted at birth and those which are initially discovered later in childhood. Thirty-two of our 40 cases were found in the newborn period, whereas 8 were first noted later in life, the age at their discovery varying from 4 months to 5 years. In all of the lesions which were noted at birth, the masses varied in size from a small nodule in the sacral-buttock area to those which were nearly half the size of the baby; in each instance, the lesion was obvious and easily recognizable because of the externally protruding lump. Conversely, those lesions which were not detected until later in infancy or childhood showed much less in the way of an external mass; they tended to be smaller and deep-seated, or else they were largely hidden in front of the coccyx and sacrum. Indeed, 2 of these initially manifested themselves as locally draining sinuses. In a few of the older children the sacral mass was red or tender, mimicking an inflammatory lesion.

Masses which were of considerable size tended to have large presacral extensions which displaced the rectum and anus forward, and usually produced partial obstruction thereof. In 2 instances, there was an even farther prolongation upward behind the peritoneum which led to partial blockage of the ureters. In no patient could a neurological defect be demonstrated in the extremities or in the sphincteric mechanism of the bladder or rectum. Although marked anterior displacement of the rectum might exist, the sphincter tone was consistently quite good.

Roentgenographic studies were carried out in 37 of the 40 cases. A soft tissue mass in the region of the coccyx was discernible in 35. The roentgenogram frequently confirmed the impression of a large retrorectal extension of the neoplasm. In 2 subjects the coccyx was involved and partially destroyed. In fresh, untreated cases there was no bony abnormality of the lumbosacral spine, but in 3 with subsequent recurrence, sacral destruction was noted at a second hospitalization. In 1 case wherein an intraspinal extension was discovered at autopsy at 15 months, films had not shown any widening of the sacral canal on multiple examinations during life.

Calcification was demonstrable in 16 of the tumors (43 per cent) and this finding when located in the presacral region was most helpful in differentiating teratomas from other retrorectal masses such as a duplication of the colon. Calcific deposits were usually amorphous, and were scattered irregularly. Rarely, a more compact or discrete shadow resembling a tooth or compact bone was seen. Calcification did not necessarily mean that the lesion was a benign one.

Intravenous pyelography was used in 5 cases, and in 1 instance (with a large intrapelvic and abdominal extension) demonstrated an advanced obstructive type of bilateral ureterectasia and hydronephrosis. Barium enema supplied little additional information in the 1 case in which it was used. Metastases to the lungs or distant skeleton were seen in the films of 6 children at some time during the course of their disease; in 4 of these such metastases were observed at the time of first admission to this hospital.

DIFFERENTIAL DIAGNOSIS

Meningocele. Inspection and palpation of the mass is the most useful step in differenti-

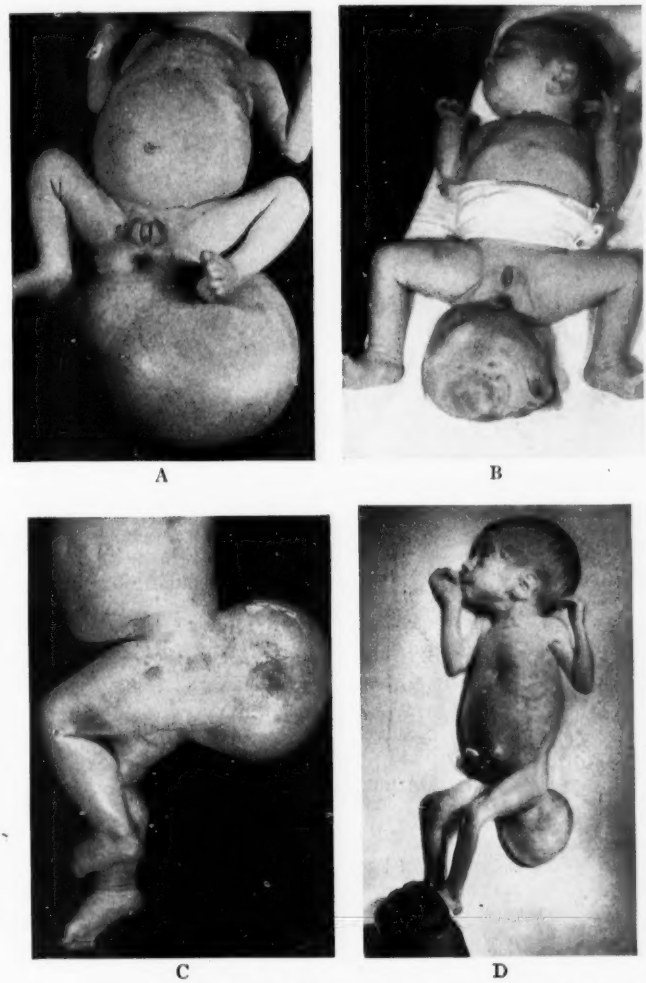
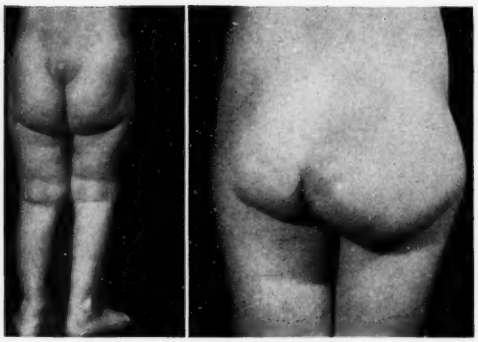


Fig. 1. Photographs of typical sacrococcygeal tumors in young babies. A, Large mass (about half cystic) with broad attachment and with marked anterior displacement of the rectum and anus. B, Moderate-sized mass, with a pedunculated stalk. C, Medium-sized mass (entirely solid), with broad attachment, and with considerable extension up in front of the coccyx and sacrum. D, Premature baby with teratoma, which was successfully removed. (Total weight 3 pounds 5 ounces.) Baby's weight after removal of tumor, 2 pounds 10 ounces.)

ating a sacrococcygeal teratoma from other lesions, particularly from a meningocele or myelomeningocele. The latter can be ruled out at once if the mass is solid or contains solid portions. However, when a mass is largely or completely cystic, the differential diagnosis may be exceedingly difficult to make; neurological defects in the legs or x-ray evidence of sacral deformity are highly suggestive of myelomeningocele, whereas the absence of these would suggest a teratoma. Deficiencies of development of the spinal cover-



A B

Fig. 2. Photographs of sacrococcygeal tumors in older children, indicating findings which are apt to be different from those seen in newborn babies. A, Child 18 months old Mass reddish and inflamed. Impression of infected pilonidal sinus led to incision and drainage, with evacuation of pus. Only later did curettage show underlying neoplasm which, in spite of removal, was followed by fatal metastases to spine and lungs. B, Neoplasm dissecting out into buttock of 10 year old girl.

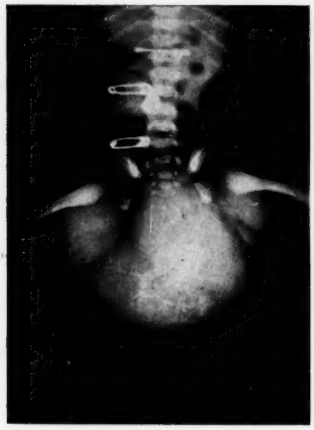


Fig. 3. Roentgenogram from a newborn baby with a large sacrococcygeal tumor with calcification therein. (Calcification does not necessarily indicate a good prognosis.)

ings are apt to produce a swelling which communicates with the cerebrospinal pathway, a point which can be demonstrated by increased tension in the mass during crying, or by bulging of a fontanelle when manual pressure is made over the mass.

Chordoma. While these may occur in this region in adults, they are exceedingly rare in early life. When they appear, they are most frequent in males and involve primarily the sacrum or tissues in front of and behind it. Arising as they do from a portion of the intraspinal remnants of the notochord, they characteristically destroy regional bone, a fact which is readily demonstrable by x-ray film, and which is rarely seen in sacrococcygeal teratomas.

Fig. 4. Roentgenogram from a 10 year old girl with a sacrococcygeal tumor, showing destruction of the coccyx and sacrum, indicative of a malignant lesion and a poor prognosis. Destruction of the sacrum is very rare in newborn babies, but it is more frequently seen in older subjects. Whenever it occurs, it almost certainly indicates a high degree of malignancy and a poor outlook.

Ependymoma. These tumors are exceedingly rare in the sacral region; they originate from ependymal cells which line the central canal of the cord. They appear in the filum terminale and grow out between the spinal arches and present themselves in the presacral area. They erode bone by pressure necrosis.

Pilonidal cysts and sinuses. While this differentiation would seem to be easy, in 2 cases (older children) we found it impossible to differentiate a small teratoma (with a draining sinus) from an infected pilonidal sinus. Only microscopic examination of biopsy material led to the correct diagnosis in each instance.

TREATMENT

Every patient with a sacrococcygeal teratoma should be offered the benefits of surgery, regardless of a large size of the mass or a small size of the patient. If skeletal or pulmonary metastases are present, obviously little will be accomplished by local excision. Since the vast majority have had no evidence

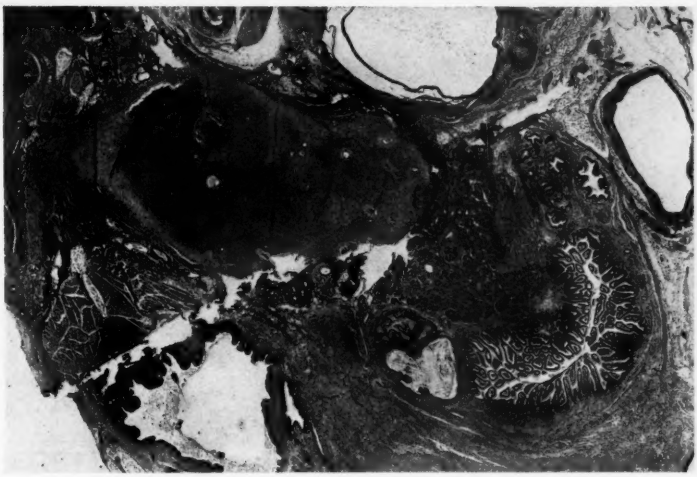


Fig. 5. Photomicrograph of section made across coccyx, showing close proximity of teratoma. Several cystic structures are seen surrounding the bone, and in right lower corner are compact cellular nests and also adenomatous structures.

of metastases, we feel that a radical attack on the sacrococcygeal mass is usually desirable. Preoperative examination of some babies might give the impression that the neoplasm surrounds the rectum or the vagina in such a way that precludes a clean operative removal, but it should be emphasized that it is universally possible to find a good plane of cleavage which will allow the mass to be dissected completely off of these structures. Prematurity has not been a contraindication to operation, a fact which has been repeatedly emphasized in our series, and an example of which is shown in Figure 1,D.

For 1 of our babies, surgery was refused by the parents. Two other patients died of intercurrent conditions (atelectasis, bronchopneumonia) before surgical therapy could be instituted. Four patients had distant metastases and were subjected only to biopsy. Three patients had been operated upon elsewhere and had recurrences when they were referred to us. All 3 of these were subjected to a secondary operation and are now well and free of demonstrable tumor.

Of the remaining 30 cases, operative removal of the teratoma was carried out; there was 1 postoperative death. In 2 cases it was necessary to perform the resection in two stages; a perineal excision was accomplished, only to find that a mass extended upward into the retroperitoneal space above the promontory of the sacrum. For each child a laparotomy was performed 2 weeks later for removal of the intra-abdominal portion. Out of the 30 patients initially treated by us there were 7 with local recurrences from 9 months to 3 years later. One of these has a tiny residual calcified mass in front of the sacrum (which has been known to exist for 15 years) and refuses further surgery. A second developed pulmonary metastases and died. Five were reoperated upon; 3 are apparently cured; and 2 have died of metastases.

While a few of the patients in the earlier part of the series had what would now be regarded as an incomplete operation, a routine procedure has now been adopted, the principal points of which are enumerated as follows and are depicted in Figures 8, 9, 10, and 11.

General anesthesia, with open drop ether, has been used for all except a few babies who were premature and for whom local novocain infiltration seemed more appropriate. In all cases it has been routine to insert a cannula (or small polythene catheter) into an arm vein prior to commencement of operation so that fluids and blood can be administered during

Fig. 6. Drawing of a sagittal section through the neural axis and attached sacrococcygeal teratoma removed at autopsy from a 4 hour old premature infant, who died of atelectasis shortly after admission to the hospital. The relationships are apparent between the superficial teratomatous mass, the coccyx, and the intraspinal extension which reached the level of the second sacral segment. (A similar intraspinal extension was found in an 11 months old infant from whom we had removed a sacrococcygeal neoplasm in the first week of life. This child subsequently died at 15 months of widespread metastases.)

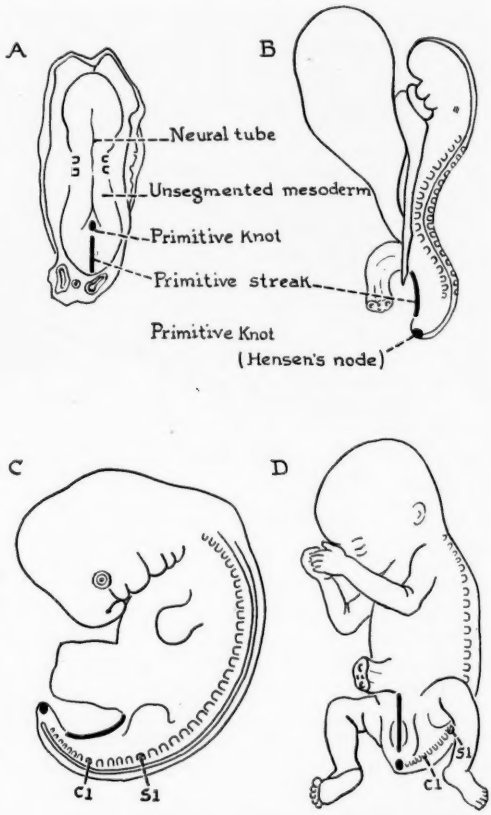


Fig. 7. Sacrococcygeal teratomas presumably arise from totipotential cells which are initially derived from the primitive knot (Henson's node). These primordial cells are most apt to be found close to the pathway traversed by the primitive knot or to its final resting place (in the sacrococcygeal area). A, The human embryo at the beginning of somite formation. The primitive knot is located at the caudal end of the neural tube. B, A 17-somite human embryo demonstrates the apparent caudal migration of the primitive knot while somites are formed and pushed cephalad. The primitive streak is now ventral. The primitive knot remains at the tip of the neural tube. C. Human embryo at the middle of the sixth week, at which time the tail is of maximal length. Forty-two somites are present, and the primitive knot is now pushed to the tip of the tail. D, The fetal form which is reached in the tenth week following the resorption of the tail (Kumitomo). Thirty-four somites including the coccyx remain.

The tail does not drop off, but a retraction of it takes place as fragmentation and resorption of the ependymal canal somites and tail-duct take place. The primitive knot comes to lie at the tip of the coccyx, and any teratoma arising from it would be similarly located.

(From J. Lewis Bremer, unpublished data).

the surgical procedure. This precaution has been very helpful in avoiding shock during long and difficult dissections, and it obviates any haste which might prevent a complete excision.

The child is placed in a face-down position, with the head turned toward one side, and the abdomen and pelvis raised over a sandbag or folded sheet so that the thighs hang and leave the teratoma projecting uppermost. A strip of vaseline gauze is packed into the rectum and left in place during operation; the presence of this intraluminal wad facilitates palpation and identification of the rectum during the subsequent separation of it from the neoplasm. The buttocks and presenting mass are prepared with a suitable cleansing agent (for which we prefer half-strength tincture of iodine), and any areas which are ulcerated must be repeatedly swabbed. The drapes are

placed in such a way that the entire mass and its base are exposed, but great care is taken to insure continuous coverage of the anus so that it is kept out of the field.

If the teratoma is attached by a small stalk, a transverse elliptical, cutaneous incision can be made around its base. In most cases the attachment is broad and it is better to make an inverted V incision, cephalad to the teratoma base; this will give the best exposure in the depths of the wound and will also keep the postoperative wound farthest away from the anus.

In cutting across the subcutaneous tissues, one often encounters a number of attenuated fascial layers which must be transected; failure to cut through these will lead to difficulty in finding a proper cleavage plane around the teratoma. When the incision has been carried down to the appropriate depth, the cuts in the fasciae and thinned-out muscles can be carried widely out over either side of the mass. This maneuver usually begins to release the mass and gives it some mobility. At this stage it is possible to see the attachments of the neoplasm to the coccyx and to see the projections of the neoplasm up into the pelvis, along which blunt dissection can now be started. The entire coccyx should be cut off from the base of the sacrum, letting it fall away with the teratoma. This step gives additional mobility to the mass, which can now be pulled slightly out of the wound, or can be displaced toward either side so that it can be detached from any intrapelvic viscera. This part of the dissection can generally be accomplished bluntly since the mass has but scanty attachments to the anterior surface of the sacrum. It is now possible to raise the teratoma out of the wound and turn it in a caudal direction so that the upper portion of the rectum is brought into view. With this clear exposure, the mass can now be carefully stripped off of the rectum from above downward. (At this stage the identification of the rectum is made much easier by the vaseline pack which had previously been inserted into it.) As the neoplasm is pulled away, it leaves in view an exceedingly long, isolated, attenuated segment of rectum. The teratoma's only attachment is by a hinged skin flap just above the anus; this

Fig. 8. Baby with teratoma, showing preoperative insertion of a plastic catheter into an antecubital vein, for administration of fluids and blood during operation.

is cut across and the neoplasm discarded. Meticulous hemostasis of the field is now effected.

The perineal structures will be seen drooping down at a level much lower than normal. To restore more normal relationships, the rectum and sagging perineal structures should be carried up toward the pelvis, a step which is accomplished by taking several sutures of silk through the levator ani muscles (just above the anus) and the presacral fascia. Tightening of these stitches will raise all of the prolapsed tissues to a satisfactory level.

The superficial parts of the wound are now appropriately closed. No muscle, however macerated or stretched out, should be sacrificed or cut away, since much of this has potentialities for subsequent function. Any excess of skin can be trimmed off in amounts and directions necessary to provide a good cosmetic contour of the buttocks. Any revision of skin edges is made with the goal of making a final skin closure as an inverted V, placed in such a way that it is as far as possible above the anus. The wound is sealed with flexible collodion before the drapes are removed. The rectal pack is pulled out.

Following operation the infant is placed in a face-down position on a Bradford frame which is well padded with foam rubber and is covered

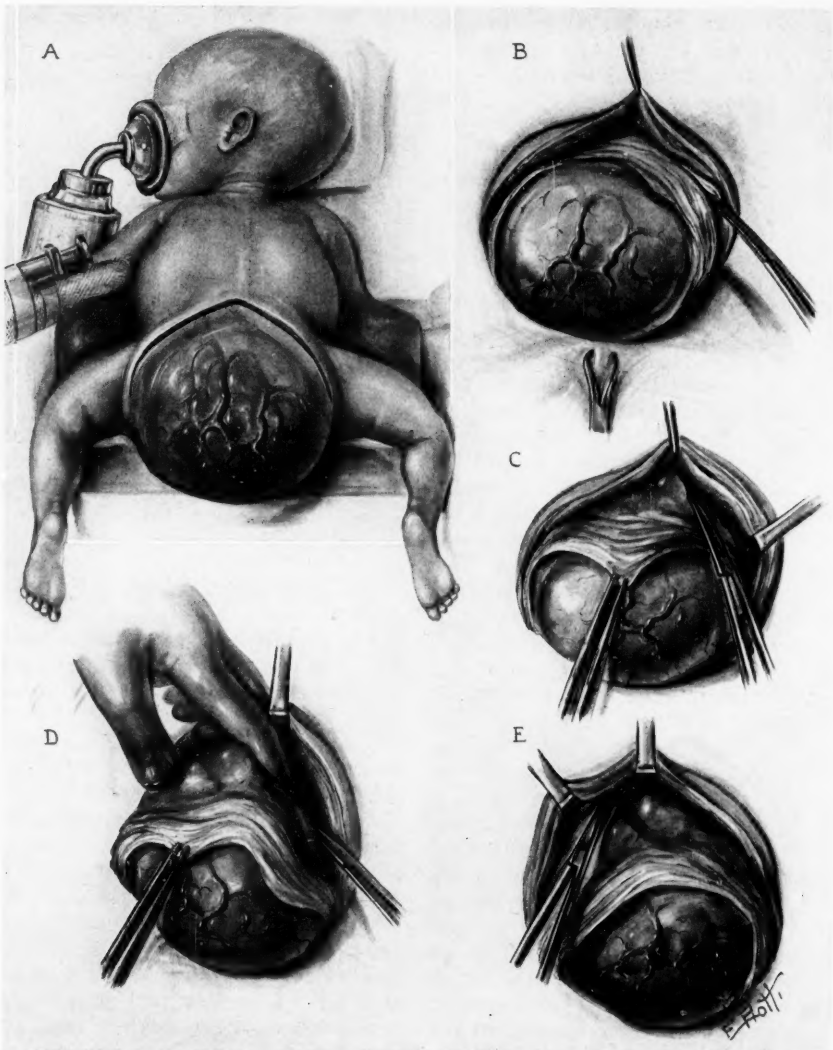


Fig. 9. Operative steps in removal of a sacrococcygeal teratoma. A, Position on table. Abdomen supported over a roll, to raise lower half of body off of table. V-shaped cutaneous incision at upper border of mass. B, Incision being developed through subcutaneous tissues and superficial fascia. C, Beginning dissection over superior portion of mass. D, Carrying dissection as far as possible along a cleavage plane. E, Sharp dissection is at times necessary to free the mass from surrounding structures.

with suitable plastic film. This position should be maintained for at least a week (or until the sutures are removed) to give the wound the best possible chance to remain clean and dry. Any urine or feces which are passed will fall forward and will not contaminate the wound. Obviously, this position will require good nursing care, in order to avoid pressure areas and points of irritation on the knees and face.

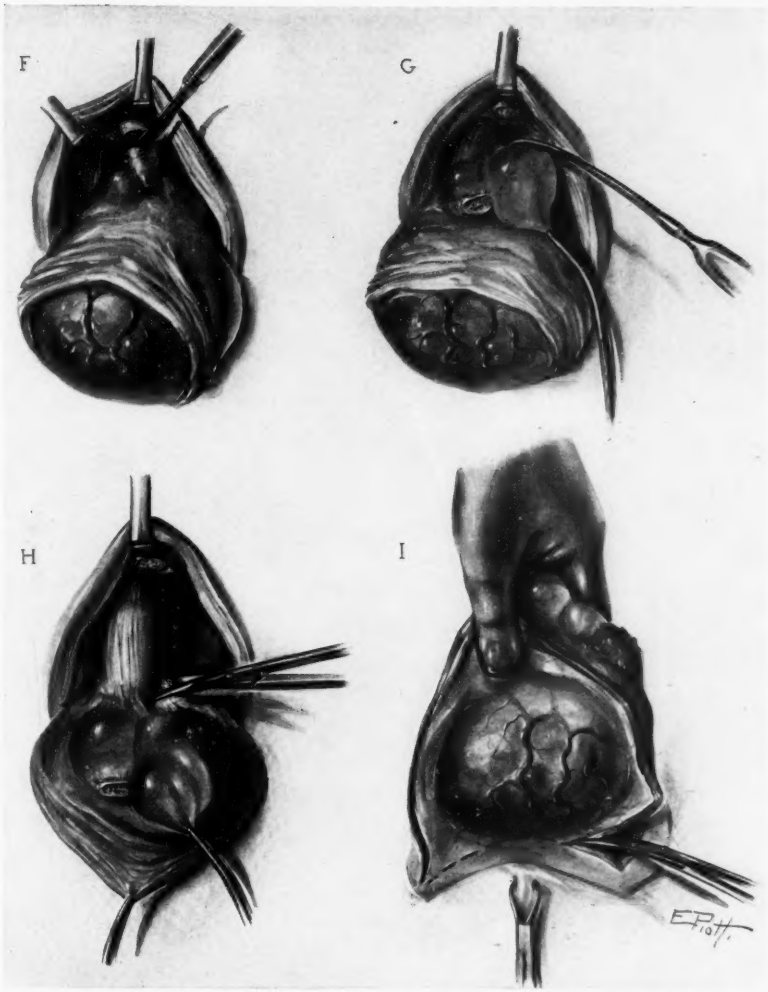


Fig. 10. Operation, *continued*. F, Entire coccyx cut away with teratoma, a most important step. G, Dissection being carried up into hollow of the sacrum. Rectum coming into view. H, Entire posterior wall of rectum exposed, the teratoma having been dissected away from it. I, Cutting cutaneous edge inferiorly, the last remaining attachment of the mass. (The towel clip is just superior to the anus and keeps this out of the field.)

RESULTS

There has been but 1 postoperative death; this was in a newborn infant who developed diarrhea on the third day and died on the fourth.

In the last 10 years there have been no wound infections; a situation which has been attributed to rigid asepsis during operation, to careful postoperative supervision of the wound, to the maintenance of a postoperative face-down position, and to the routine prophylactic use of antibiotics.

While the extensive surgical freeing and isolation of the rectum would bring apprehension about the possibility of subsequent anal dysfunction, we have not encountered rectal or

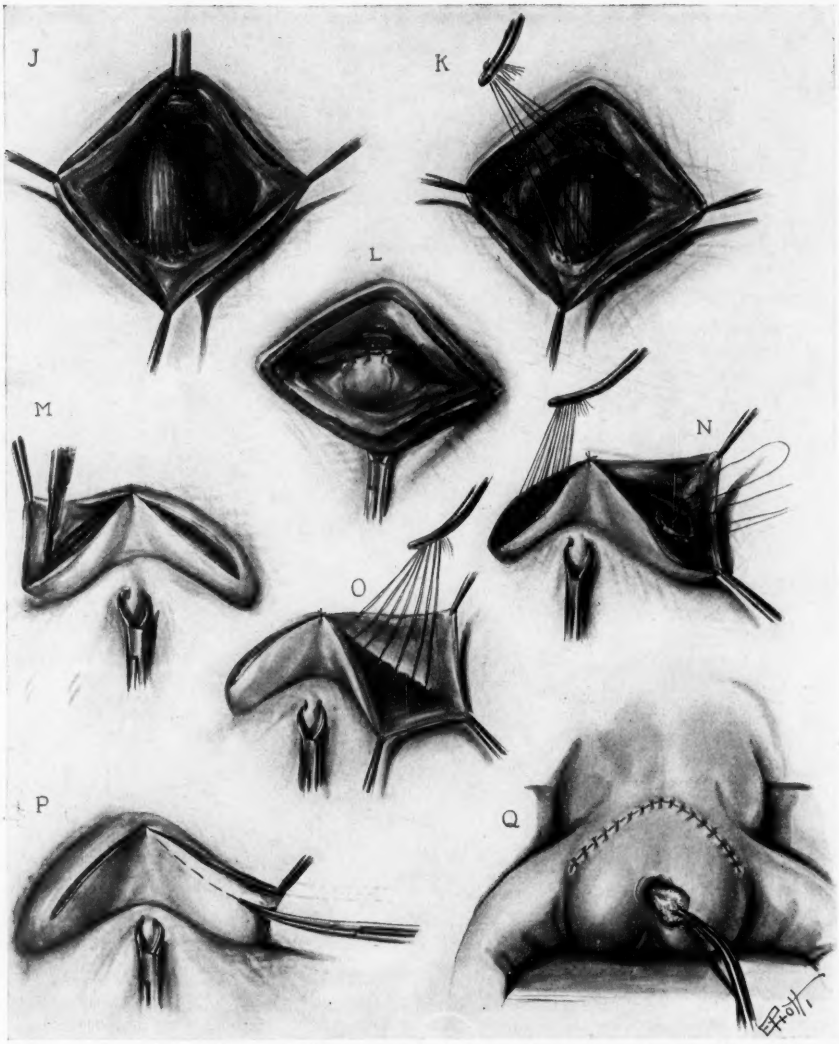


Fig. 11. Operation, *continued.* J, After removal of the teratoma, the rectum remains widely exposed throughout its entire length. K, To bring the anal area up to a normal position, the perianal tissues (base of the levator ani muscles) are brought to the presacral fascia with several silk sutures. L, Supporting sutures tied. M, Apex of skin sutured into an inverted V. N, Excess skin being dissected away from underlying gluteus muscles. (All muscle is saved no matter how much it is frayed out.) O, Suture of muscles being completed. P, Excess skin being trimmed away. Q, Skin closure completed. Vaseline gauze pack being removed from the rectum.

urinary incontinence in any case. There have been no complaints referable to the excision of the coccyx.

It seems desirable to separate the 40 cases of the series into two groups, of 32 cases occurring in newborn infants and 8 which were initially recognized in older babies and children.

In the younger group of 32 patients there were 3 for whom no operation was under-

taken (1 refused operation and 2 died of intercurrent disease), leaving 29 babies who were treated by removal of the mass. Following these 29 radical attempts, 1 baby died on the fourth postoperative day (from overwhelming diarrhea), and 2 have died of malignant recurrences (10 months and 19 months respectively after operation). This leaves 26 subjects who are living and well without demonstrable tumors for periods varying from 2 years to as long as 28 years. Four of these 26 patients have had secondary removal of local recurrent tumor and are free of disease for 2 years, 3 years, 4 years, and 8 years respectively. In summary, of the 32 patients in this younger group, there was an operative attack in 29 and there is an overall salvage of 26 who are alive and are presumably rid of their disease.

In the older group of 8 patients, 4 had distant metastases prior to admission, so that only a biopsy was done to confirm the diagnosis. For the remaining 4 patients, 3 of whom had had previous operation elsewhere, radical attempts were made to remove the sacrococcygeal mass. Of these 4 radical attempts, the results were as follows: 1 had a recurrence in 14 months, at which time there was an unsuccessful attempt to remove the regrowth and there was death within 1 year from widespread metastases. One patient had recurrence 3 times for which 3 subsequent operations were done and the child is now apparently free of tumor 3 years after the last procedure. One patient had a recurrence for which reoperation was done, and is now well 3 years later. One patient had no recurrence after the primary operation and is well 2 years later. In summary, of these 8 patients in the older group there are 3 who have been salvaged and are apparently free of their disease.

Combining the statistics of the two groups, there is a total of 40 patients with an over-all salvage of 29 subjects who are now apparently free of neoplasm. From our figures it is obvious that the outlook is far better for the sacrococcygeal teratomas in the newborn group than in older subjects.

A review of our material leaves no doubt about the great importance of total resection of the coccyx during removal of a sacrococcygeal teratoma. In 19 cases in which the coccyx was not resected, or was only partially excised, there were 7 recurrences, a rate of 37 per cent. In 10 cases in which the coccyx was completely resected there have been no recurrences.

While every attempt should be made completely to enucleate one of these growths without breaking through its encircling capsule, the accidental opening into tumor tissue or into cysts does not always militate against a favorable outcome. In at least 9 of our operations, the surgeon was conscious of the fact that cysts had been entered or tumor had been cut across; there was only 1 recurrence in this group.

A local recurrence of a mass does not necessarily imply an ultimately fatal issue, and further attempts at removal of local tumor should always be undertaken if no metastases are apparent. In 7 cases, secondary operations were carried out. In 6 of this group there have been survivals and apparently permanent cures; in the 1 remaining case 3 secondary operations were performed before all of the growth could be eradicated.

Pathologic examination of these neoplasms does not necessarily predict accurately the prognosis in any given case. Some of these tumors have contained highly malignant tissues of various sorts and have been followed by long-term cure. It is worthy of note that those neoplasms which were composed predominantly of neural elements were three or four times more likely to be followed by recurrence than was the case in the other tumors in which all three germinal layers were more extensively represented.

The fact that intraspinal extensions of neoplasms were found in 2 of our cases raises the question of whether examination of the spinal canal by x-ray visualization with opaque substances would be desirable in all patients. It is of course possible that such routine study might disclose more instances of such intraspinal extension when it is not otherwise suspected. However, it is our opinion that the intraspinal injection of pantopaque is not justified or indicated in every fresh case (particularly in the newborn group), but

we are inclined to believe that all patients with any regional recurrence should be examined in this way.

SUMMARY

Sacrococcygeal teratomas are most frequently encountered in infancy and early childhood. They are much more common in females. The growth may reach enormous size, compared to the size or weight of the patient. Radical attempts should always be made to remove these growths, regardless of their large size and regardless of the young age, or even prematurity of the host. The entire coccyx should always be excised along with the neoplasm, because microscopic nests of neoplastic cells are commonly found in or immediately adjacent to this bone.

A series of 40 patients from our clinic is presented. There have been no deaths during operation on these babies or children. Thirty-two of the subjects were in the newborn period, of whom 29 were operated upon and 26 of these are alive and are apparently rid of neoplasm. Eight of the subjects were older babies or children, of whom 3 are apparently free of neoplasm. Of the entire 40 subjects there is an over-all salvage of 29 who are presumably cured. The outlook is far better for sacrococcygeal teratomas in the newborn group than in the older subjects. An optimistic attitude should be adopted toward sacrococcygeal teratomas, particularly in babies, because there is adequate proof that the vast majority of these subjects can be cured if prompt and adequate surgical removal is undertaken.

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PERINEOTOMY

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PERINEOTOMY is a perineal plastic operation designed to increase the size of the vaginal introitus. Indications for its use are clear cut, but cases requiring such a procedure are not frequently encountered. When properly used and properly performed it gives excellent anatomical and symptomatic results. This presentation is concerned with indications for perineotomy, the details of the procedure, and the results obtained in 42 private patients upon whom the operation was performed during the years 1940 to 1949 inclusive.

The indications for perineotomy are (1) dyspareunia due to congenital deformities of the perineum and hymen, (2) dyspareunia due to scars of the vulva and perineum, (3) congenital or acquired abnormalities of the perineum, vulva, and hymen, discovered premaritally, which will interfere with normal coitus, and (4) chronic leucorrhea and vaginitis due to poor vaginal drainage.

In some women the perineum may be of unusual thickness, height, and firmness. In others, the hymen may be unduly thick and fibrous with a single small opening or multiple small fenestra. As a result of these congenital abnormalities penile pressure is either unable to effect an entrance or fails to dilate the introitus to a point where pain is no longer experienced. If entrance is accomplished the penis may be deviated anteriorly so that the urethral meatus is repeatedly and distressingly traumatized. Rarely, an abnormally large penis will cause distress even though the introitus is of normal diameter.

Distortion of the perineum and vulva from previous surgical procedures or from injuries may produce distressing dyspareunia. Painful episiotomy scars and too tight repairs of the perineum at the time of vaginal plastic procedures are common examples of such problems. "Picket fence" injuries to the perineum from a fall astride a sharp object may result in marked cicatrization of the vulva and perineum making subsequent coitus difficult or impossible.

It is generally agreed that severe pain as the result of coital trauma in early marriage may create lifelong dyspareunia and frigidity. In order to avoid such unhappy situations, most young women coming for premarital consultation should undergo a pelvic examination. Occasionally one of them will reveal abnormalities of the vulva, hymen, or perineum which will render coitus unduly painful. In selected cases a perineotomy, performed several weeks prior to marriage, will avoid a distressing, difficult, and, perhaps, traumatic ordeal when intercourse is attempted.

Patients whose chronic leucorrhea and vaginitis are due to poor vaginal drainage are most unusual. However, there is the rare instance in which an intractable discharge and a chronic vaginitis are the result of pocketing of secretions above a tight hymen and a high perineum. In such cases a perineotomy is indicated to improve vaginal drainage but it should be resorted to only after nonsurgical efforts at relief have failed.

The operation. Perineotomy is a relatively simple surgical procedure but certain principles should be adhered to if the results are to be uniformly satisfactory. In most instances simple incision of the hymen is not sufficient, for the size of the introitus depends more upon the height of the perineum than on the width of the hymen. Usually, when the hymen is thick and firm, the perineum will be high and rigid. In order to insure adequate relaxation of the perineum, and coincident enlargement of the introitus the perineum must be incised deeply in the midline. The operator's left forefinger in the rectum serves as a guide for the perineal incision and protects the rectum (Fig. 1). The incision is necessarily made dorsally through

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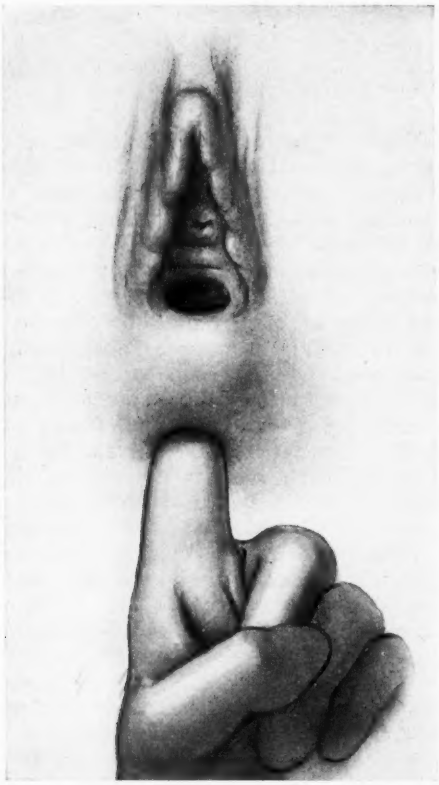

Fig. 1. Perineotomy. The operator's left forefinger in the rectum puts the rigid perineum under tension, serves as a guide for the perineal incision, and protects the rectum.

Fig. 2. Perineotomy. The incision is made dorsally through the hymen, through the perineal skin toward the anus, through the perineal body, and through the posterior vaginal mucosa to a point well above the hymenal ridge. (Figures 2 to 5 from Curtis-Huffman, *Textbook of Gynecology*, W. B. Saunders Co,. 1950.)

the hymen, through the perineal skin toward the anus, through the perineal body, and through the posterior vaginal mucosa to a point well above the hymenal ridge (Fig. 2). As the incision is made in the perineum, the muscle fibers will be seen retracting laterally. Traction with Allis forceps placed at the sides of the incision puts the tissues under tension. Scissors dissection separates the vaginal mucosa from the underlying muscle (Fig. 3). The hymenal ridge which is adherent to the fascia and muscle must be separated laterally and the vaginal mucosa freed sufficiently to allow it to be mobilized without tension. It is essential that good hemostasis beneath the mucosal flap be secured to prevent the formation of a postoperative hematoma. Interrupted anteroposterior fine chromic catgut (No. 0000) sutures unite the vaginal mucosa to the perineal skin (Fig. 4). The underlying muscle is not sutured.

At the completion of the operation the divided hymen forms two curtain-like lateral folds and the vaginal mucosa a trough-like floor for the introitus (Fig. 5).

There is a minimum of postoperative discomfort. Patients are allowed out of bed as soon as they recover from the anesthesia. Occasionally there will be slight but inconsequential separation of the suture line. Gentle cleansing of the perineum with moist cotton after voiding avoids injury from toilet tissues

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 3. Perineotomy. Traction with Allis forceps placed at the sides of the incision puts the tissues under tension. Scissors dissection separates the vaginal mucosa from the underlying muscle.

Fig. 4. Perineotomy. Interrupted anteroposterior fine chromic catgut sutures unite the vaginal mucosa to the perineal skin.

Fig. 5. At the conclusion of the perineotomy the divided hymen forms two curtain-like lateral folds and the vaginal mucosa a trough-like floor for the introitus.

and keeps the parts clean. The patient is examined 10 days following operation and the wound inspected. If healing has been satisfactory, she returns once or twice weekly for gentle digital vaginal examination. Intercourse should not be permitted until she realizes that the examiner can insert two fingers in the vagina without causing discomfort. When coitus is begun adequate lubrication through the use of a lubricating jelly and slow penile entrance will reduce discomfort. When examined several months after operation, the vaginal introitus is patulous, the remnants of the hymen fall to each side, and the perineal scar is practically invisible (Fig. 6). The operation does not interfere with subsequent labor, episiotomy, nor perineal repair.

Results. Excellent results (Table I) have been obtained in the 42 patients operated upon during the past 10 years. It will be noted that dyspareunia was the indication in 32 of the 42 cases, and that postoperative relief of coital pain was obtained in 28 patients. Actually, of the 4 cases not listed as relieved, 3 could not be followed and only 1 constituted a known failure. Patients in whom dyspareunia was due to injuries or scars of the vulvar and perineal tissues are not included in the series if vaginal plastic procedures were done in addition to a perineotomy, or in whom a technique other than that described was used.

Details of the various types of abnormalities or injuries will not be given. The following single case reports selected from each group of patients are illustrative of the problems encountered.

Case 1. Mrs. A. G., aged 24 years, married 3 years, had never been able to have coitus because of perineal pain. Her husband, aged 26 years, who had had no difficulty in premarital coitus, found entrance impossible. With continued unsuccessful attempts he developed first premature ejaculations, later partial impotence. He had extramarital coitus on 2 occasions without difficulty. Examination of wife revealed a firm, unyielding, very thick intact hymen with 0.5 centimeter aperture near urethra, and a high rigid perineum. Perineotomy was performed in 1947. Thereafter, normal coitus without dyspareunia was possible. In 1949 the patient had a normal pregnancy and labor.

Fig. 6. Photograph of patient 4 months after perineotomy. The introitus is patulous, the remnants of the hymen fall to each side, and the perineal scar is almost invisible.

CASE 2. Mrs. V. N., aged 50 years, married 21 years, had been subjected to a hymenectomy 1 year after marriage because of dyspareunia. She had never been able to have coitus because of severe perineal pain on attempted entrance. Her husband was healthy; he had no urological problems. Examination of the wife showed: introitus would admit one finger snugly; perineum was firm, high, and thick; hymen was absent; exquisitely tender hymenectomy scar was present. Perineotomy was performed in 1948. Follow-up study showed that she could have normal coitus without pain.

CASE 3. Miss A. P., aged 21 years, was to be married in 8 weeks. Premarital examination showed an unusually firm, thick hymen with two apertures, neither of which was more than 0.4 centimeter in diameter. It was impossible to introduce examining finger into vagina because of pain and apprehension. Perineotomy was performed in 1949. After marriage she was able to have normal coitus, with no dyspareunia and excellent libido.

CASE 4. Miss C. A., aged 32 years. Intractable vaginitis and leucorrhea had been present for 2 years and had resisted all medical attempts at relief. Examination revealed a firm hymen with aperture which would admit one examining finger. Pocket above hymen held approximately 2 cubic centimeters of mucopurulent secretion. Marked vaginal hyperemia was present. Vaginal discharge showed mixed type of bacteria, no trichomonads, no fungi. Perineotomy was performed in 1950. One month's treatment of vaginitis with simple douches (lactic acid) and sulfanilamide cream was carried out. Recovery was uneventful and there has been no recurrence.

DISCUSSION

Perineotomy is primarily intended for the relief or prevention of dyspareunia due to anatomical abnormalities or pathologic lesions of the perineum and vulva. Unfortunately, problems of coital pain may be extremely complex due to the merging of organic and psychic factors. A painstaking history with emphasis on the details of the sexual act and a meticulous examination, which must often be repeated before the site of the pain is localized, are frequently necessary before the specific cause for the discomfort can be determined. In many instances, the primary complaint of dyspareunia will not be obtained at the first visit, for women are reluctant to discuss the intimacies of their sexual life or have been led to believe that painful coitus is unavoidable. For that reason specific inquiry relative to dyspareunia is often a pertinent part of the gynecological history when the complaints are ill defined.

TABLE I.—INDICATIONS FOR AND RESULTS OF PERINEOTOMY IN 42 PATIENTS

Indications	No. patients operated upon	Good result	Poor result	No follow-up
Dyspareunia due to congenital factors	26	23	1	2
Dyspareunia due to scars or injuries of perineum	6	5	0	1
Factors discovered premaritally	8	6	1	1
Leucorrhea, vaginitis from poor vaginal drainage	2	2	0	0

Usually, after a careful history and examination, an organic basis for dyspareunia will be discovered, for the vast majority of women suffering from painful coitus have a physical lesion causing their discomfort. When that lesion has been shown to be a high perineum, rigid hymen, or distortion of the introitus from scars or injuries, a perineotomy will relieve the distress. No patients are more grateful than those women who, after years of unhappy conjugal existence due to dyspareunia, have been cured by perineotomy.

A great many women have some pain with defloration. Under natural circumstances this "honeymoon dyspareunia" is not severe and disappears within a short time. However, unsuccessful attempts at initial coitus,

or forceful entry by an inept or rough partner, or oft repeated coitus through a traumatized hymen becomes a distressing experience and its association with discomfort becomes fixed. In some individuals such experiences create a functional dyspareunia which persists after the introitus has become adequate in size. As a consequence, fear of pain and aversion to coitus are developed.

Avoidance of such an unhappy chain of consequences can be accomplished by premarital instruction of the bride and groom, and by perineotomy in those selected cases in which it is evident that rigid tissues will interfere with the initiation of normal sexual life.

SUMMARY AND CONCLUSIONS

The indications, technique, and results of perineotomy, an operation designed to increase the size of the vaginal introitus, are presented.

Indications for the operation are dyspareunia due to congenital deformities of the perineum and hymen, dyspareunia due to scars of the vulva and perineum, congenital and acquired abnormalities of the perineum, vulva, and hymen discovered premaritally which will interfere with normal coitus, and chronic leucorrhea and vaginitis due to poor vaginal drainage.

Excellent results were obtained in 36 of the 42 patients who were operated upon; there were 2 failures and 4 patients could not be traced.

While patients requiring perineotomy are not frequently seen, the operation when properly used and properly performed gives excellent anatomic and symptomatic results.

A COMPARATIVE STUDY OF OPERATIONS FOR CARCINOMA OF THE RECTUM AND RECTOSIGMOID

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SURGICAL removal is unquestionably the most effective treatment at this time for the majority of carcinomas of the rectum and rectosigmoid. Complete extirpation of the malignant tumor, accomplished with the lowest hospital mortality rate, the least physical and psychologic morbidity and re-establishment of intestinal continuity, if possible, must be strived for whenever possible. The level of the lesion, the extent of local and distant involvement, the general condition of the patient, and surgical judgment all are factors that govern the selection of the procedure considered best suited to accomplish these ends.

Ultimately the 5 year survival rate is the most important criterion of success of any operation for carcinoma. Sufficient time has not elapsed to determine this factor for patients undergoing the various operative procedures in conjunction with recent advances in care before, during, and after operation. We considered it advisable, however, to examine the hospital mortality rate after various operations for carcinoma of the rectum and rectosigmoid at the Mayo Clinic during a 5 year period. In addition, certain other factors subsequent to one stage and multiple stage anterior resections for carcinoma in these locations during this same period are compared.

MATERIAL AND METHODS

Our study included cases of carcinoma in which, in the opinion of the surgeon at the time of operation, the growth was situated in the rectum or rectosigmoid; the growths were located at or below the level of the peritoneal reflection. The hospital deaths which followed three general types of operative procedures used in treatment of carcinoma in these locations during the period 1945 to 1949 inclusive were studied and compared.

The first group was comprised of 689 cases in which one stage combined abdominoperineal resection was performed. Included in this group is a small percentage of cases in which the surgeon performed some type of "pull-through" operation.

The second group included 277 cases in which the surgeon considered the lesion resectable and in which a two stage resection was intended. The first stage in this group consisted either of performing the abdominal portion of an abdominoperineal resection, or performing a sigmoidal loop colostomy alone. The second stage consisted of resection of the lesion through a posterior approach.

The third group included 352 cases in which anterior resection with primary end-to-end anastomosis, with or without preliminary or concomitant proximal colostomy, was performed.

The histories of the 352 patients who had undergone anterior resection for carcinoma of the rectum or rectosigmoid were studied and divided into two groups. The first group consisted of 151 cases in which a one stage anterior resection without a proximal colostomy was performed. The second group consisted of 201 cases in which anterior resection for carcinoma of the rectum and rectosigmoid with preliminary or concomitant proximal colostomy was performed. Hospital mortality rate, number of operative procedures, and average days of hospitalization in the two groups were compared. The cases in which anterior resection was performed as a palliative procedure were further analyzed.

RESULTS OF STUDY

The results of our study of hospital deaths after the three general types of operative procedure are presented in Table I. There

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TABLE I.—OPERATIONS FOR CARCINOMA OF THE RECTUM AND RECTOSIGMOID: MORTALITY

Year	One stage combined anterior-posterior resection			Two stage posterior resection			Anterior resection		
	Patients	Hospital deaths		Patients*	Hospital deaths		Patients	Hospital deaths	
		Number	Per cent		Number	Per cent		Number	Per cent
1945	144	2	1.4	67	5	7.5	53	3	5.7
1946	164	8	4.9	52	1	1.9	50	1	2.0
1947	128	8	6.2	55	4	7.3	68	2	2.9
1948	123	5	4.0	51	3	5.9	90	6	6.7
1949	130	5	3.8	52	0		91	2	2.2
Total	689	28	4.1	277	13	4.7	352	14	4.0

*Includes 14 cases in which only the first stage was completed.

was considerable but inconstant variation in the mortality rate by year in each of the three groups. The principal cause of death in each operative procedure is shown in Table II; peritonitis, pulmonary embolus, and pneumonia accounted for the majority of the cases.

In the group of 689 cases in which one stage combined abdominoperineal resection was performed, there were 28 hospital deaths (4.1 per cent).

Of the 277 resectable cases in which a two stage operation, with posterior resection as the second stage, was contemplated, there were 13 hospital deaths (4.7 per cent). An analysis of these deaths by stage of operation is presented in Table III. In 14 of the 277 cases only the first stage of the operation was completed. Ten of these patients (3.6 per cent of 277) died after the first stage; 4 were not considered able to tolerate further surgical intervention, 2 because of cardiac difficulties, 1 because of a complication of the urinary tract, and 1 because of pulmonary tuberculosis. The first 3 patients received radium therapy; the fourth patient was transferred to a sanatorium without further treatment of the rectal carcinoma. There were 3 deaths (1.1 per cent) in the group of 263 patients who underwent the second stage of the posterior resection.

Fourteen deaths (4.0 per cent) occurred in the group of 352 cases in which anterior resection, including both one stage and multiple stage procedures, was performed.

TABLE II.—OPERATIONS FOR CARCINOMA OF THE RECTUM AND RECTOSIGMOID: PRINCIPAL CAUSE OF DEATH

Cause of death	One stage combined anterior-posterior resection	Two stage posterior resection		Anterior resection		
				One stage	Multiple stage	
		First stage	Second stage		First stage	Last stage
Peritonitis	11	5	1	4	2	
Pulmonary embolus	6	1	1		4	1
Pneumonia	2	2		1		
Pseudomembranous ileocolitis	2				1	
Coronary disease	2					
Vascular collapse	1	1	1			1
Uremia	1					
Subhepatic abscess	1					
Pyelonephritis	1					
Debility	1					
Myelitis		1				
Total	28	10	3	5	7	2

As shown in Table IV, 5 hospital deaths (3.3 per cent) occurred in the group of 151 patients who underwent one stage anterior resections. Nine deaths (4.5 per cent) occurred in the group of 201 patients who had multiple stage anterior resections. Two deaths (1.0 per cent) in the latter group followed closure of the colostomy.

A comparison of the number of operative procedures and the average number of days of hospitalization in one stage and multiple stage anterior resections is presented in Table V. Including operative procedures necessary for postoperative complications, there were 162 procedures performed on the 151 patients who underwent one stage anterior resection, an average of slightly more than 1 operation for each patient. In 3 instances it was deemed advisable to perform a proximal colostomy subsequent to what was intended to be a one stage anterior resection; 1 patient died. There were 555 operative procedures performed on the 201 patients who had multiple stage anterior resections, an average of 2.8 operations for each patient. The usual patient under-

TABLE III.—TWO STAGE POSTERIOR RESECTION FOR CARCINOMA OF THE RECTUM AND RECTOSIGMOID: MORTALITY

Patients	Hospital deaths					
	First stage		Second stage		Total	
	Number	Per cent	Number	Per cent	Number	Per cent
277	10	3.6	3	1.1	13	4.7

going a multiple stage anterior resection had three procedures: anterior resection with a concomitant transverse colostomy, application of clamps to the spur of the colostomy, and, finally, closure of the colostomy.

The average number of days of hospitalization for patients on whom a one stage anterior resection was performed was 22.7 days, in comparison with an average of 52.6 days of hospitalization for patients undergoing multiple stage anterior resection.

An analysis of the cases in which anterior resection was performed as a palliative procedure for carcinoma of the rectum or rectosigmoid is presented in Table VI. These patients had definite metastasis to the liver or so extensive local spread that it was impossible to remove all the carcinoma. There were 19 cases in each group, which comprised 12.6 per cent of the one stage anterior resections and 10.6 per cent of the multiple stage anterior resections. There was 1 death (5.3 per cent) in each group. The average number of days of hospitalization was 26.2 days for those patients on whom a one stage anterior resection was performed and 48.7 days for those patients who had multiple stage anterior resection. There were 20 operative procedures on the 19 patients on whom a one stage anterior resection was performed, and 47 operative procedures on the 19 patients on whom multiple stage anterior resection was performed. In the latter group, 3 patients, aside from the 1 patient who died while hospitalized, did not have the colostomy closed.

COMMENT

There is no unanimity of opinion at the time of our study as to the choice of operative procedure which satisfies the objectives of eradicating carcinoma of the rectum and rectosigmoid. Such factors as proximal, lateral, and retrograde spread are being investigated. There continues to be controversy as to the adequacy of such sphincter-saving operations as anterior resection and the several modifications of the "pull-through" procedure. Even the adequacy of the one stage combined abdominoperineal resection is questioned. On the other hand, it remains to be shown that the two stage resection, with wide posterior resection as the second stage, is more effective.

It is not intended to imply that the three general types of operation for carcinoma of the rectum and rectosigmoid compared in this study can be used interchangeably in every case. Obviously anterior resection cannot be employed for lesions at or just above the dentate margin. The judgment of the surgeon, after evaluation of all factors, however, determines which of two or more possible procedures is chosen. It is worth while to make a comparative study of those factors which can be evaluated at this time. A further evaluation of the cases in these three groups is planned for the future when sufficient time has elapsed to obtain 5 year survival rates.

In recent years many important advances have been made in the preparation of patients for operation on the large intestine, as well as in care during and after the operation. The blessings of antibiotic drugs, sulfonamide drugs, adequate transfusions of whole blood, improved anesthesia, and careful fluid and

TABLE IV.—ANTERIOR RESECTION FOR CARCINOMA OF THE RECTUM AND RECTOSIGMOID: MORTALITY

Year	One stage resections			Multiple stage resections		
	Patients	Hospital deaths		Patients	Hospital deaths	
		Number	Per cent		Number	Per cent
1945	19	1	5.3	34	2	5.9
1946	18	0		32	1	3.1
1947	29	1	3.4	39	1	2.6
1948	38	2	5.3	52	4	7.7
1949	47	1	2.1	44	1	2.2
Total	151	5	3.3	201	9	4.5

electrolyte balance during the 5 year period concerned in this study, are well appreciated. It is considered that these three groups of patients treated during this recent period can be compared, but they are not comparable to those groups of patients having undergone similar operations previously under different circumstances.

Comparison of the results in this study reveal that the over-all mortality rate is satisfyingly low and is essentially the same after each of the three operations for carcinoma of the rectum and rectosigmoid. The mortality rate varies considerably in each group from year to year; the average mortality rate for the 5 year period, however, is considered to be more significant than the rate for any 1 year.

One stage and multiple stage anterior resections particularly are amenable to comparison, since they are performed for similar lesions and should be equally adequate in removing the carcinoma. Some surgeons performed one stage anterior resection in most cases, other surgeons performed multiple stage anterior resection in most cases, and still others selected one or the other of these procedures according to what they considered advisable in each case. Generally a multiple stage operation with a concomitant proximal colostomy, as was performed in the majority of cases in this group, was chosen because it was considered by the surgeon to be the safest procedure for the patient. Results of this study showed a mortality rate of 3.3 per cent for the one stage anterior resection and of 4.5 per cent for the multiple stage anterior resection. The difference between these mortality rates, however, is not thought to be significant. Nevertheless, it is apparent that one stage anterior resection, in which careful anastomosis is made without tension, is as safe a procedure as multiple stage anterior resection. The slightly higher mortality rate after multiple stage anterior resections is accounted for by 2 deaths which followed closure of the colostomy.

TABLE V.—ANTERIOR RESECTION FOR CARCINOMA OF THE RECTUM AND RECTOSIGMOID: MORBIDITY

Year	One stage resections			Multiple stage resections		
	Patients	Number of operative procedures*	Average days of hospitalization	Patients	Number of operative procedures	Average days of hospitalization
1945	19	23	26.8	34	95	59.0
1946	18	18	25.1	32	87	61.4
1947	29	31	27.3	39	108	56.3
1948	38	39	22.3	52	135	50.9
1949	47	51	20.7	44	130	51.1
Total	151	162	22.7	201	555	52.6

*Includes operative procedures necessary for complications following one stage anterior resection.

TABLE VI.—PALLIATIVE ANTERIOR RESECTIONS FOR CARCINOMA OF THE RECTUM AND RECTOSIGMOID

Anterior resection	Patients			Palliative operations with hospital deaths		Average days of hospitalization	Number of operative procedures
	Total	Undergoing palliative operations					
		Number	Per cent	Number	Per cent		
One stage	151	19	12.6	1	5.3	26.2	20
Multiple stage	201	19	10.6	1	5.3	48.7	47*
Total	352	38	10.8	2	5.3	37.5	67

*In 3 cases, in addition to the 1 hospital death, the colostomy was not closed.

Since the mortality rate is essentially the same, the morbidity in these two groups of anterior resection assumed considerable importance. Physical and psychologic trauma to the patients is increased with each operative procedure. The difference between an average of 22.7 days of hospitalization after one stage anterior resection and an average of 52.6 days of hospitalization subsequent to multiple stage anterior resection represents an additional 30 days of hospitalization. In many instances this additional economic burden is a real problem for the patient, the hospital, and the surgeon.

In those instances in which anterior resection is performed as a palliative procedure the objectives are to remove the primary or "feeder" growth and to restore normal intestinal continuity in order that the patient may be as comfortable as possible during the remainder of his life. Our study has shown that the mortality rate was the same in these

groups of palliative one stage and multiple stage anterior resections. The significant increase in duration of hospitalization, the number of operative procedures, the unpleasantness of a temporary colostomy and the additional economic burden make the multiple stage anterior resection a less desirable procedure especially for these patients.

SUMMARY AND CONCLUSIONS

The mortality rates have been determined for three types of operation performed for treatment of carcinoma of the rectum and rectosigmoid at the Mayo Clinic during the period 1945 to 1949 inclusive. The difference in hospital mortality rates of one stage combined abdominoperineal resection (4.1 per cent), two stage resection with the second stage as a posterior resection (4.7 per cent) and anterior resection (4.0 per cent) was not significant. The results indicate that the afore-mentioned two stage operation with posterior resection does not have a lower mortality rate than the other procedures.

Comparison of the mortality rate after one stage anterior resection (3.3 per cent) with that of multiple stage anterior resection (4.5 per cent) indicates that a one stage operation is at least as safe as a multiple stage procedure.

Since the mortality rates of one stage and multiple stage anterior resections are similar, the increased physical, psychologic, and economic trauma which results from extended hospitalization and multiple operative procedures makes multiple stage anterior resection a less desirable operation. This is especially true in those instances in which anterior resection is performed as a palliative operation.

The success of operative procedures in all cases in this study will be determined when sufficient time has elapsed to provide the necessary information.

PARENTERAL NUTRITION

XII. The Successful Intravenous Administration of Large Quantities of Fat Emulsion to Man

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SEVERAL studies concerning the intravenous use of emulsions of fat in man have been reported from this laboratory (6, 9). It was shown that emulsions containing 15 per cent of fat could be given safely in moderately large quantities to a variety of patients without any adverse reactions. The utilization of the fat in such an emulsion was also demonstrated to reverse a negative nitrogen and potassium balance in a patient maintained on a diet low in protein and inadequate in calories (6).

The purpose of the present paper is to report on the successful intravenous administration to severely ill, and in most cases emaciated, patients of emulsified fat in amounts larger than those used in previous studies. Some preliminary data are also presented which concern the rate of removal of the fat from the blood stream, the level of ketones in the blood, oxygen consumption, and respiratory quotient during and following administration of the emulsion.

EXPERIMENTAL

The emulsion used in these studies was similar in composition to that used in earlier investigations (6). It contained 15 grams of coconut oil, 0.5 gram of a soybean phosphatide preparation (fraction BF_2 made from asolectin, 3), 1.0 gram of demal-14, and 5 per cent dextrose solution to make 100 cubic centimeters. Homogenization was accomplished under nitrogen by high pressure homogenization. The emulsion was filtered directly from the machine using positive nitrogen pressure, and was collected in sterile infusion bottles. While still hot, the emulsion was sterilized by autoclaving for 15 minutes at 15 pounds per square inch, and then stored at 24 degrees C. in the dark. The emulsion was tested for sterility, pyrogens, and possible toxicity by the procedures previously described (6). If all of these tests gave negative results, the emulsion was considered satisfactory for use in clinical studies. Emulsions prepared with ingredients of questionable pyrogenicity may turn out to be unsatisfactory for clinical use. For reasons as yet not completely understood, various batches of asolectin do not give a satisfactory BF_2 preparation.

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CLINICAL STUDIES

Initial clinical use of a new batch of emulsion was made according to the following procedure and only after careful laboratory studies (6) had been satisfactorily completed. All infusions were administered through disposable plastic tubing. The emulsion was first used in a patient who had previously received earlier batches of an emulsion. Five hundred cubic milliliters of emulsion were administered at a rate of about 5 milliliters per minute and oral temperatures were taken at frequent intervals. Close clinical observation was constantly maintained and the usual measurements such as blood pressure, pulse, and respiration rates were made. If the first infusion was uneventful, a second infusion was given the next day to the same patient in the same manner except that 1,000 milliliters were given. If this infusion was uneventful, the emulsion was then used in clinical cases in

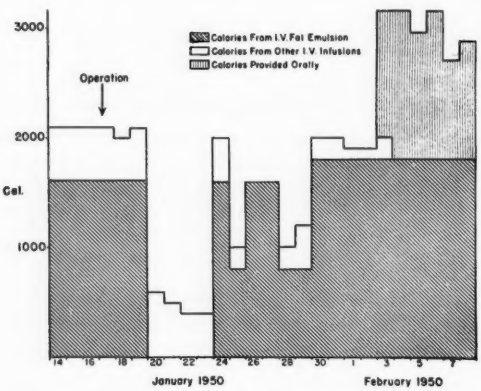

Fig. 1. Caloric intake over 26 day period. Patient R7646, gastric ulcer, subtotal gastrectomy, splenectomy, partial pancreatectomy.

which an inadequate caloric intake existed. When the emulsion was given to a new patient, the precautions previously listed were also taken. The usual rate of infusion was approximately 8 milliliters per minute after patient tolerance had been demonstrated.

Table I summarizes the results of a series of 9 severely ill patients who received 1 liter or more of the fat emulsion. The case histories of 4 patients who received a number of large (1,000 c.c.) infusions are discussed in greater detail.

PATIENT R7646 was a 67 year old spinster with a long-standing gastric ulcer invading the pancreas. After a total gastrectomy, splenectomy, and partial pancreatectomy her postoperative course was stormy. Caloric intake, preoperative and postoperative, was most inadequate. She lost 6 kilograms from her maximum weight of 42 kilograms. The patient was given caloric supplements of intravenous fat amounting to approximately 1,600 calories per day for 22 days during a 26 day period. Figure 1 shows the distribution of calories provided to this patient in the form of intravenously administered nutrients, including fat emulsion, and food during the preoperative and postoperative periods. During most of this period, her nonfat caloric intake was virtually nil; the emulsions were well tolerated, and her final recovery was in part traceable to the caloric supplementation provided by the fat. Weight change was not striking during the administration of fat, but thereafter she gradually regained 2.4 kilograms, the weight gain beginning toward the end of the period of fat administration.

PATIENT OE92 was a 70 year old white widow suffering from progressive anorexia, weight loss, and hematemesis. A tentative diagnosis of inoperable carcinoma of the stomach was confirmed by laparotomy. Because of the patient's inadequate oral intake, she was given intravenous fat emulsion on 10 of 12 postoperative days. The patient had 1 febrile reaction with temperature of 103 degrees 4½ hours after the completion of one of her infusions of 1,000 cubic centimeters of intravenous fat emulsion. It was not established beyond doubt that this was due to the fat. Her other 9 infusions were uneventful. On several occasions vomiting occurred during an infusion, but it is doubtful that this was due to the fat emulsion since the patient vomited frequently at other times. The patient's oral intake of food was virtually nil and yet her weight of 43 kilograms was maintained throughout the infusion period. The total amount of emulsion administered was 10 liters which provided a total of 16,000 calories. This patient's illness terminated fatally due to progression of her disease and continued intestinal obstruction. Death occurred about 2 weeks after the cessation of fat therapy. At postmortem there was no evidence by visceral examination of any abnormal deposition of fat in parenchymatous organs.

PATIENT 2D755 was a 67 year old white married male, admitted with marked and progressive weight loss due to self-imposed dietary restrictions and postprandial emesis. Laparotomy disclosed a large retroperitoneal sarcoma which was inoperable. During a 19 day period, preoperative and postoperative, he received 14 infusions (14 liters) of fat emulsion and on no occasion was any reaction evidenced. Caloric intake from all other sources during this period was estimated as less than 500. His weight showed no significant change. On the fifth postoperative day, the patient suddenly collapsed as he attempted to get out of bed. He expired within an hour. The clinical impression was that of a cerebrovascular accident. Permission for a postmortem examination was refused. The patient had not received parenteral fat on the day before or the day of death. The fat infusions were given to this patient in the hope of improving his nutrition sufficiently for discharge to a hospital for chronic care. His cerebral vascular accident occurred before discharge could be arranged.

PATIENT 5B866 was a 52 year old white male admitted with jaundice and a presumptive diagnosis of carcinoma of the pancreas which was confirmed by laparotomy. After considerable preparation a Whipple operation was carried out on the thirty-second hospital day. Nutritional difficulties arose during the postoperative period due to ileus and intestinal obstruction. A jejunostomy was performed. Ten intravenous infusions of fat emulsion were given over a period of 20 days without any adverse reactions of any kind. The patient was discharged on the sixty-fourth hospital day. Body weight was maintained during this period. Although many therapeutic procedures were carried out during this period, including jejunostomy feeding, the additional 16,000 calories provided by the fat played a signifi-

TABLE I.—SUMMARY OF PATIENTS WHO RECEIVED 15 PER CENT FAT EMULSION INTRAVENOUSLY IN DAILY AMOUNTS OF 1 LITER OR MORE

Patient No.	Diagnosis	No. of infusions*	Changes in temperature, pulse, respirations, or other signs of reaction
R7646	Gastric ulcer, total gastrectomy, splenectomy, partial pancreatectomy**	21	None
OE92	Gastric malignancy with obstruction**	10	None
2D755	Retroperitoneal sarcoma**	14	None
5B866	Carcinoma of pancreas**	10	None
5B974	Carcinoma of stomach, total gastrectomy	1	None
B1634	Terminal nephritis	1	None
M1751	Terminal carcinoma of cervix	2	None
2D742	Fractured pelvis, carcinoma of right colon with resection	2	None
6C324	Lye burn of esophagus	3	None

*Each infusion amounted to 1 liter except in the case of Patient No. 2D755 who received several 1.5 liter infusions.
**See individual case description.

cant role in convalescence. The infusions were well tolerated despite borderline liver function due to common duct obstruction.

As part of the present study, preliminary investigations were made on the blood ketone concentrations, oxygen consumption, and respiratory quotient during and following the intravenous administration of fat emulsion to man. Blood samples were taken at intervals for the determination of acetone, acetoacetic acid, and B-hydroxybutyric acid by a colorimetric method (1, 7). The concentration of infused fat in these blood samples was determined turbidimetrically. The results of such a study in a normal healthy volunteer adult male are shown in Figure 2.

RESULTS

The infusion of 1 liter or more of a 15 per cent fat emulsion was well tolerated by the series of 9 patients as can be seen from the data in Table I and the case histories which are representative of the series. No reactions of any kind were observed in any of the subjects; the occasional vomiting of Patient OE92 was probably not attributable to the

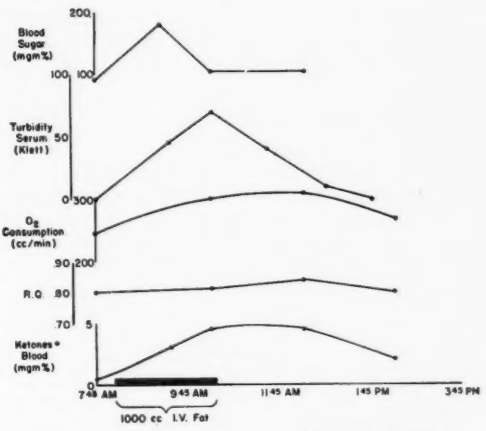

Fig. 2. Data obtained from a normal adult male volunteer (Subject A.J., aged 26 years) to whom 1,000 milliliters of a fat emulsion furnishing 1,600 calories were administered at a constant rate of infusion.

emulsion since frequent vomiting occurred on days when no fat was given. The 4 patients who received from 10 to 21 infusions of emulsion, each totalling 1 liter or more, showed no adverse effects to the repeated intravenous feedings. Despite the critical nature of the illness, the usual weight loss was not observed during the periods that fat emulsions were infused to provide adequate calories. As can be seen from Figure 1, Patient R7646 was supplied with approximately 1,600 calories per day in the form of the fat emulsion for 22 out of a 26 day period. During this same period, the calories supplied by all other means were less than one-third of this amount except during the final days of the study when oral intake of food was again possible. She received the fat emulsion before, on, and after the day of operation. The 4 days during which no emulsion was given were caused by a temporary inadequate supply of the emulsion.

The data presented in Figure 2 were recorded from an infusion experiment in a normal volunteer in which 1,000 milliliters of fat were administered, at a constant rate of infusion. The concentration of infused fat in the blood stream increased until the infusion was terminated. The amount of fat then decreased and returned to a normal level in

approximately 3 hours. The concentration of total ketones in the blood rapidly rose during the infusion and began to decrease within an hour after the end of the infusion. These results demonstrate the rapidity with which the emulsified fat is removed from the blood and undergoes metabolism. There was a slow rise in oxygen consumption but little change in respiratory quotient, the latter possibly explainable on the basis of an initial low value and because the emulsion also contained carbohydrate.

DISCUSSION

Properly prepared emulsions of fat can be administered in relatively large amounts to patients without any adverse reactions. Quantities of a 15 per cent fat emulsion of 1 liter or more caused no effects on blood pressure, pulse, respiration, or temperature in a variety of clinical cases. The repeated daily infusion of emulsion did not cause reactions to develop locally or systemically. As illustrated by Figure 1, the calories supplied by such means are considerable especially when compared with the number of calories which can be supplied to such patients by ordinary methods.

The utilization of the fat in such emulsions was indicated by the maintenance of body weight, and by the increased concentration of blood ketones during and following an infusion as shown in Figure 2. The rapid rise in blood ketones was best demonstrated by Patient R7646 whose blood ketones rose from 0.5 milligram per cent to 13 milligrams per cent following 500 cubic centimeters of intravenous fat emulsion. Urinary ketone excretions rose from 1 milligram during a 6 hour period previous to the infusion to 58 milligrams during a 6 hour period starting with an infusion of intravenous fat. No harmful effects were observed at any time that could be attributed to the ketosis or ketonuria; these phenomena are regarded merely as measurable evidence of the degradation of triglyceride to smaller carbon fragments in its catabolism to water and carbon dioxide with the liberation of 9 calories of energy per gram.

The rapidity of the utilization of fat administered in this manner has been clearly demonstrated in the rat (2, 8) and dog (5) by the use of triglycerides labeled with carbon 14. Shafiroff and associates have recently reported studies with humans given 15 and 20 per cent fat emulsions stabilized with gelatin. These emulsions also contained glucose and a protein hydrolysate at concentrations approximating 5.4 and 3.0 per cent respectively. They concluded that fat emulsions of this concentration had to be given with considerable caution and interpreted their high incidence of increases in body temperature to be due to the rapidity with which the fat was oxidized. The studies reported in the present paper and in a previous report (6) *do not* support these conclusions. First, many patients have been given large quantities of the 15 per cent fat emulsion described in the present paper without adverse reactions of any kind. Second, although the fat in the emulsions used in the present study is rapidly oxidized, *no* temperature rise occurred in any of the patients. In previous reports (6, 9), it was shown that a rise in temperature will result when the emulsion is *pyrogenic*. A chill may or may not accompany the rise in temperature. Third, the experience in this laboratory and of others[1] has clearly shown that commercial oils are pyrogenic and that the pyrogens must be removed prior to making the emulsion. Fourth, the temperature regulating mechanisms of the body and the economy of physiologic energy production and utilization argue against a rise in body temperature being caused by the oxidation of the fat. Indeed, some of the most rapid energy-exchanging mechanisms, such as thyrotoxicosis, result in only trivial or negligible changes in body temperature.

Another discrepancy between the studies reported by Shafiroff and associates and those presented here lies in the time curve of the concentration of fat in the blood during an infusion of emulsion. They reported that the concentration of fat in the blood, as measured by the chylomicron technique, increased initially during the infusion and then decreased even though the rate of infusion was equal to or greater than before. This phenomenon has never been noted in this laboratory. Instead,

[1]Personal communications.

the blood fat concentration has always been found to increase steadily during an infusion of constant rate and to decrease only when the infusion was terminated. Only when the infusion rate is lowered sufficiently can the concentration of blood fat be decreased during the infusion. Further studies are necessary to clarify the differences between the results from the two laboratories.

Further studies on the clinical application of emulsions of fat are under way. It is clear from both the present and previous data (6, 9) that emulsified fat can safely be given to patients and such fat is utilized for energy purposes.

SUMMARY

1. Intravenous administration of a 15 per cent fat emulsion in large quantities to 9 severely ill patients caused no serious adverse reactions.

2. Four of the patients received 10 to 21 one liter infusions. All maintained their body weight during the infusion period.

3. Preliminary observations are reported on the concentrations of blood fat and ketones, oxygen consumption, and respiratory quotient, during and after an infusion of fat emulsion.

4. Emulsions improperly prepared, stored too long, or containing pyrogenic substances will cause febrile reactions with regularity; such febrile reactions may not be ascribed to cryptic metabolic disturbances until common pyrogenic factors have been absolutely excluded.

5. It is concluded that properly prepared emulsions of 15 per cent fat can be administered safely to patients, and fat so administered is readily utilized for energy purposes.

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EDITORIALS

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MARCH, 1951

THE USE AND ABUSE OF ANTIBIOTICS IN THE TREATMENT OF SURGICAL INFECTIONS

ONLY those who have been practicing surgery for more than ten years can fully appreciate the change that has taken place in the course of surgical infections following the availability and clinical application of the antibiotics. This change has been more rapid and more dramatic than that which took place in the course of postoperative infections before and after Lister. It took almost twenty years for Lister's principles to be generally accepted by surgeons. Still more years passed by before surgeons were sufficiently confident of the results obtained with aseptic technique in operating rooms to expand the field of surgery and to perform operations in areas of the body previously considered inaccessible. On the other hand, in less than five years the rapid development of the field of antibiotics has almost completely changed our methods of dealing with potential as well as established surgical infections.

Pharmaceutical companies, working together under government subsidy, and stimulated by the requirements of war and the pressure exerted by the War Production Board and the Committee on Medical Research of the Office of Scientific Research and Development, found ways and means within a very short time to produce penicillin cheaply and in rapidly increasing quantities. First the casualties of war and then the civilian population benefited from these efforts. In the last five years almost every doctor has been able to demonstrate that with the use of penicillin, he can check the progress of many infections which formerly spread rapidly beyond his control, causing extensive destruction of tissue, prolonged or permanent disability, or death.

It is often stated that the availability of the antibiotics for everyday use has not changed any of the fundamental principles in the treatment of surgical infections, but it is my considered judgment that even some of our fundamental principles have been changed. It used to be considered axiomatic that wherever there was a collection of pus, surgical drainage was called for, and in certain circumstances complete excision of the diseased area was essential to control the spread of infection or to save the patient's life. Now in many cases of surgical infection, by the use of antibiotics, surgical procedures may be completely obviated or conservative surgical procedures may succeed in cases which formerly would have required radical treatment. Now aspiration of pus may take the place of incision, or limited excision may take the place of complete removal.

The application of Lister's principles to the operating room caused the disappearance of erysipelas and pyemia following clean operations. Now erysipelas and pyemia are almost never seen either following well established spontaneous infections or following operations in contaminated areas. Formerly, if infections developed following operations on the heart or on the brain, they were almost always fatal, but now such infections rarely occur, or if they do, when treated specifically and promptly, many are brought quickly under control. Following operations on the lung, where moderate contamination of the field often resulted in fatal infections, now they seldom occur, and in surgical procedures along the alimentary tract, particularly on the esophagus, which is contaminated by a mixture of mouth organisms, resection can be done with a minimal incidence of infection. Furthermore, primary resections of the bowel may be carried out in one rather than in multiple stages. These changes in our experience are due, in large measure, to the antibiotics.

The discovery of penicillin and the demonstration of its ability to control clinical infections, immediately stimulated large numbers of bacteriologists and chemists to explore this newly opened field. Gradually the clinicians found that penicillin was not a panacea, and the laboratories were able to demonstrate that many organisms are resistant to penicillin, while others are able to produce an inactivating penicillinase.

These findings intensified the search for antibiotics that would succeed where penicillin failed. As a result of these labors, we now have six antibiotics which are sufficiently low in toxicity that they may be given systemically in doses which are clinically effective and at the same time relatively harmless to the patient. These are in the order of their discovery: penicillin, streptomycin, bacitracin, aureomycin, chloromycetin, and terramycin. None of the last five can be given in such unlimited dosage as penicillin, which is so abundant and so cheap that it is now used indiscriminately and often unintelligently.

The extent to which penicillin is used may be judged by the fact that during the past year 76 billion units were distributed from the hospital pharmacy for patients in the Columbia-Presbyterian Medical Center (New York) and its cost was approximately 50 per cent of the total drug bill. At the same time all of the other antibiotics are being used in increasing quantities. The same conditions probably apply to all hospitals and to the general practice of medicine outside of hospitals. For economy's sake constant vigilance is necessary to be sure that these agents are not wasted, and for the patients' sake intelligence must be used to insure the prompt employment of the most effective agent.

If we are to give the patient the full benefit of all of the knowledge we have obtained in our appraisal of antibiotics, it is essential that the causative organism of his infection be determined and that the agent most effective in inhibiting the growth of this organism be applied at the earliest possible time. This requires the close co-operation of a bacteriology laboratory, and while the general practitioner may be justified in using these antibiotics empirically by trial and error, every surgeon, who must depend upon a hospital for an operating room, should demand at the same time the services of a laboratory qualified to solve his bacteriological problems.

There is no excuse, therefore, for any surgeon to treat a patient with any antibiotic until he has made an effort to find out the nature of the causative organism and its susceptibility to the available antibiotics. Specimens of exudate should be obtained in as large a quantity as possible from the local lesion and

also from the blood, if there is any indication of systemic spread. This material should be sent at once to the laboratory for the appropriate study. A preliminary report on the probable nature of the causative organism and the appropriate antibiotic can usually be given in twenty-four hours or a little longer, if there is a bacterial mixture which will require separation of the individual elements.

In acute cases the initial treatment need not wait for this bacterial analysis, but the antibiotic most likely to succeed may be tried first, depending upon the knowledge and experience of the surgeon in the treatment of similar cases. However, if the laboratory's study indicates that another antibiotic or a combination of antibiotics will be more effective, an immediate shift should be made to the best form of treatment. In chronic cases of long standing, the laboratory studies should be made before any new antibiotic treatment is started. Often the laboratory will find in such cases that the organisms are resistant to those agents which have been previously used.

This editorial is a plea to all surgeons to utilize to the full the facilities of the bacteriological laboratory to bring infections under prompt control, instead of blindly and unintelligently pumping in antibiotics, one after another or in "shotgun" fashion, to no avail.

FRANK LAMONT MELENEY.

RADIOACTIVE ISOTOPES IN SURGERY

THE application of radioactive isotopes to the problems of medical research antedated the earliest rumblings of the atomic bomb. Biological work with artificially produced isotopes began several years before the first accounts of atomic fission (1939). The development of the bomb has focussed public attention upon medical isotope research to an inordinate degree; the production of isotopes in the uranium pile has placed peacetime medical research in the military realm; and the public has been led to a premature expectation of practical results. The explosions over Japan have added other curious aspects to this otherwise quiet and peaceful form of scientific research.

It is a natural American tendency—and we would like to think it a tendency of the human race in general—to see a silver lining under every dark cloud. The dark aspects of the atomic bomb have been widely publicized. The realization that something incredibly disastrous had been wrought (and might be wrought again) has spurred the search for a lighter side. This more happy aspect of atomic fission is to be found in the application of isotopes to medical research. Scarcely a day passes without some comment in the newspaper about the clinical application of isotopes, the knowledge which they will give us and the cures which they will accomplish. The medical fruits of artificial radioactivity are considered as a counterbalance to the destructiveness of the atomic bomb.

This apparent connection between benefit and destruction is purely fortuitous and highly unfortunate. The same production process which makes heavy elements fissionable also makes the lighter elements radioactive. Were it not for this cohabitation in the nuclear reactor, it would be valid to state that the atomic bomb has nothing whatsoever to do with biological research using radioactive elements. Biological research with radioactive material is a natural outgrowth of chemical and physical knowledge which began to accumulate in the 17th and 18th centuries and which in the 19th century laid the groundwork for our present concepts of the structure of molecules and living tissue. Throughout this long development, the biologist has ac-

cepted any tools placed in his hands and has applied them toward his own good ends. Such research is for the good of mankind; but such goodness is in no sense a counterbalance to the atomic bomb. The bomb is a late-comer to the field and must seek the counterbalance to its horrors in the field of politics.

There are other aspects lent to isotope research by this finding of a military application for nuclear fission. The most disturbing at the present time is the security problem. There is a need for medical investigators to speak out on this security problem because only in that way will men in public life gain an understanding of our point of view.

The security problem, in final analysis, is that of keeping military secrets away from an enemy. In order to accomplish this, secrets have to be kept under lock and key. The key must be given only to individuals who can be trusted. As a principle and as a procedure this is as old as the Trojan horse. The problem is: what constitutes a secret, what a key, and who is to be trusted?

The application of isotopes to ordinary medical problems in no sense constitutes a key to the understanding of new weapons. As to the question of who is to be trusted, no one can predict where knowledge will come from. The only manner in which such knowledge can be fostered is to give the maximum number of young men the broadest opportunity for free development of their ideas. Extensive security procedures for selecting personnel will only debar from the isotope laboratory a Langerhans of our generation destined to pass along the key to important secrets—the secrets of malignancy, heart disease, poliomyelitis, not of thermonuclear weapons.

Surgical research with isotope tracers cannot be separated in any sense from similar investigations in medical, biochemical or biophysical laboratories; they all are engaged in a study of biology, normal and morbid. Startling *clinical applications* have been few: radioiodine in the diagnosis and treatment of thyroid hyperfunction; radiophosphorus in polycythemia and leukemia, and in the localization of brain tumors; radiosodium in the study of vascular disease. This list will grow and prosper but its growth is not essential—it is a by-product.

The *growth of knowledge* about diseased biological processes is far more important, and here the list is too long to recount. A few of the high spots: radiocarbon studies as an indicator of the stepwise degradation and resynthesis of carbohydrate and fat, heavy nitrogen studies on the dynamic equilibria within the "protein pool" and with particular reference to metabolism in tumors, radioiron as a measure of bone marrow function in the presence of sepsis, radioiron-tagged erythrocytes as a measure of the red cell mass in burns, radiosodium measurements of the extracellular phase in burns, shock and sepsis, radiosodium studies of the peripheral circulation, radiopotassium measurements of cell permeability and of the total body potassium, heavy water transfer as an index of water exchange and for the measurement of total body water, radiophosphorus studies of the pancreatectomy inhibition of fat phosphorylation in the liver . . . and so on for many pages. Here is the contribution of this new biophysical tool: the re-evaluation of a whole area of molecular information in atomic terms.

Let us therefore keep separate in our minds isotope research and atomic weapons; possibly we can educate our legislators to keep security-as-a-criterion-of-fitness out of the medical picture. We must not be too eager for the direct practical application of isotopes in the clinic. Surgical therapy will thrive, well-nourished on the biological information the isotopes give us. FRANCIS D. MOORE.

Chirurgische Klinik

im k. k. allgemeinen Krankenhause in Wien.

Saal 16 № 328 № I. 18 87

Name: Keller Theresia Wohnort: Hottmans 170

Alter: 43 J. Geschäft: Hausbesitzersgattin

Aufgenommen: 25. Jänner Entlassen: 20. 2. 87.

Krankheit: Carcinoma ventriculi (pylori)

Datum | Anamnese. | Ordination

Patientin 43 Jahre alt, verheiratet, will seit October 1880 über heftige Schmerzen in der Magengegend, Erbrechen, Appetitlosigkeit und Abmagerung leiden, welche fast jeden Tag, anhaltend, die Patientin bis heute quälen, häufiges, fast täglich mehrmaliges Erbrechen, seine Farbe bräunlich-grünlich, nimmt an Quantität ab. Der Harn normal, Stuhlgang regelmässig, aber verstopfend wirkende Mittel nöthig. Appetit gering. Patientin ist sehr abgemagert, Gesichtsfarbe blass, Haut trocken, Turgor gering. Die Palpation des Abdomens schmerzhaft, besonders in der Magengegend. Percussion ergibt tympanitischen Schall. Die Auscultation des Herzens und der Lungen ergibt normale Verhältnisse. Die Untersuchung per rectum ergibt nichts Abnormes. Die Untersuchung per vaginam ergibt nichts Abnormes. Die Untersuchung per rectum ergibt nichts Abnormes. Die Untersuchung per vaginam ergibt nichts Abnormes.

Krankenhaus Nr. 23. — Papierzeitung Nr. 4.

Fig. 1. Photograph of front page of history of first patient to receive successful pylorectomy for carcinoma, operated upon by Theodore Billroth.

First Successful Pylorectomy for Cancer.—Alexander Brunschwig and Edith Simandl.

THE SURGEON'S LIBRARY

THE BOOK SHELF

FIRST SUCCESSFUL PYLORECTOMY FOR CANCER

The Case History

ALEXANDER BRUNSCHWIG, M.D., F.A.C.S., and EDITH SIMANDL, M.D.,
New York, New York

THE first successful partial gastrectomy for carcinoma of the pyloric region performed by Theodore Billroth is one of the great events in modern abdominal surgery. The clinical record of the patient is still preserved in the second surgical clinic of the medical school of the University of Vienna. Its translation was made possible through the kindness of Professor Wolfgang Denk, the present incumbent of the chair of surgery, once held by Billroth. The free translation follows and it is our opinion that its publication will be of interest to those American surgeons interested in the history of surgery. The record comprises 21 pages in all. A perusal of the daily clinical notes affords a vivid impression of the postoperative treatment of that day. Parenteral fluid administration was unknown at the time of this operation, anesthesiology was in a primitive stage, antiseptic, rather than aseptic, technique was followed, the x-ray had yet to be discovered, clinical chemistry was nonexistent. Diagnosis was based entirely upon clinical signs and symptoms. Postoperative treatment was superficial and symptomatic in the light of present knowledge.

CASE HISTORY

Front sheet reproduced in Figure 1

"*Anamnesis.* This 43 year old patient had, without any known reason, a severe attack of vomiting soon after her noontime meal about the middle of October, 1880. Since then she has vomited several times daily even though food was not ingested. At present there is vomiting once a day about half an hour to one hour after a meal. So far there have been no special pains while vomiting and the act of vomiting has always been of short duration. The vomitus consisted of the eaten food and, as Dr. Breuer reports, the patient had vomited coffee ground masses on one occasion and had had tarry stools.

"Since the patient is taking very little food, the vomiting too occurs less frequently and also there are less stools. The patient has hardly any pain, she feels, as she thinks, healthy. There is only a sensation of general weakness and exhaustion. The previously well nourished Woman is said to have lost weight quickly during the previous 6 weeks and to have noticed herself a hard mass around the umbilicus under her thin and flabby abdominal wall.

"The patient had had smallpox of a mild degree when she was 17 years of age and 5 years ago she had a left puerperal mastitis which perforated spontaneously and was healed completely after 4 weeks. The onset of menstruation took place at the age of 15; there had always been a strict regularity in her period and a heavy flow, but lately this became very slight. The patient had given birth to 10 children and nursed all of them herself. Eight of these children are still alive and healthy. The patient's father is alive and healthy, her mother died of a puerperal infection.

"*Present status.* Female of average height, appearing severely emaciated and anemic, both breasts are small and flabby, the left breast showing a scar. The entire integument is very pale (white) and dry. The examination of the pelvic organs shows nothing abnormal. The lower abdomen is concave, the abdominal wall very flabby and thin, showing multiple transverse folds and wrinkles particularly in the lowest part of the abdomen. While lying flat and breathing quietly, a round prominence can be seen through the abdominal wall at the level of the umbilicus and a little to the right of it, which seems to be in connection with a second prominence to the left of the umbilicus, thus showing the outlines of the stomach. The pyloric region of the stomach appears to be distended. Upon palpation, the tumor to the right of the umbilicus appears to be rather solid and sensitive to touch, the size of a small apple, easily displaceable and not adherent to the abdominal wall. Above the solid tumor one is able to obtain a diminished resonance; above the other prominence to the left of the umbilicus representing the fundus of the stomach, one is able to get a completely tympanitic resonance. The latter tumor feels like a tense bladder. There were no other abnormal findings in the abdominal organs. When walking the patient becomes nauseated and dizzy quite often and vomits all nourishment within 1 hour. The pulse is weak and accelerated, the tongue moderately furred. The patient retains cold sour milk in small portions very well. Temperature in the evening 38 degrees C.

From the Memorial Hospital Center for the Treatment of Cancer and Allied Diseases, New York.
Dr. Simandl is a Rockefeller Foundation Fellow.

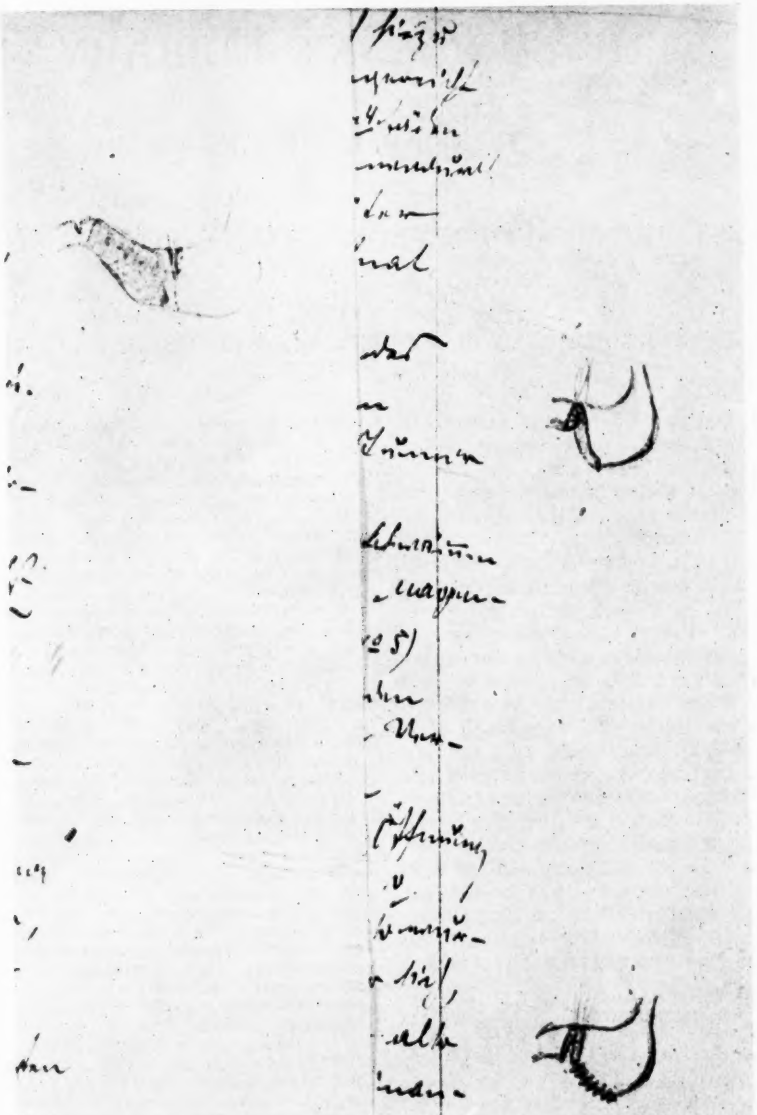

Fig. 2. Marginal notes on history sheets showing type of operation for excision of pylorus. The duodenum was united to the upper portion of the gastric wound and the lower portion of the latter was closed.

"January 27th: Normal temperature; vomited once.

"January 28th: Several enemas ordered in preparation for intended operation. Temperature in the evening 38.2 degrees C. Small bowel elimination.

"January 29th (1881): At eight o'clock in the morning a washing out of the stomach with luke warm water was performed. A long, average diameter drainage tube, rounded at one end and greased well, was put through the esophagus into the stomach and then a glass funnel was attached to the other end of the tube. One to one and a half liters of water were poured through this funnel into the stomach and before the remainder of the water in the funnel drained into the stomach, the funnel was lowered and by siphonage the water within the stomach was allowed to flow back. This procedure was repeated as many times (14 liters of water were used) as necessary until the water returned completely clear. This procedure did not cause the patient any special pain. One hour later the following operation was performed on this patient.

"*Record of operation* (see marginal sketches—Fig. 2). Under *chloroform anesthesia* and antiseptic precautions (without spray), after the temperature in the room had been brought to 25 degrees, femurs and both lower extremities of the patient were dressed with flannel slacks and boots, a transverse slightly curved (downward) skin incision measuring 11 cm. in length was made directly over the tumor extending across the linea alba. After division of the thin abdominal wall, the peritoneum was incised and divided with the pointed bistoury. After this, by manual examination, it was possible to feel the tumor involving the whole pyloric region, and the tumor together with the rest of the stomach was pulled out into the wound. A prolapse of the remaining intestines was prevented by placing well disinfected warm napkins over them. After this, the detachment of the peritoneum at the lesser and greater curvature of the stomach was begun. At the limits of the extension of the tumor and a little beyond, the adherent peritoneum was separated from the lesser curvature with five, and, from the greater curvature, with six separate ligatures en masse, a medium size (English No. 4) carbolic acid treated silk being used. During this procedure a hazelnut size tumescent mesenteric lymph node was found in the region of the pylorus (at the greater curvature), which was extirpated together with two other small nodes on the peritoneum. The tissue surrounding these extirpated formations appeared indurated. Now the duodenum, which had been pulled out of the wound, was halfway incised 1.5 centimeters below the limits of the tumor. The stomach walls were incised in the same manner on the opposite side of the tumor (at the lesser curvature), however, in normal tissue. Napkins and sponges protected the peritoneal wound and cavity from contact with gastric secretions. Four long silk sutures were placed through the healthy wound edges of the stomach wall by needles (through serosa, muscularis but not mucosa) and the wound margins of the stomach held by an assistant. The incision through the stomach walls was then extended to the greater curvature (always within normal tissue) so that at this point the tumor appeared detached. After the corresponding wound edges of the stomach and duodenum were brought toward each other, the previously mentioned four sutures through the stomach wall were then placed with needles through the wound edges (muscularis and serosa) of the duodenum and, while turning the wound margins in, were tied one after the other. These sutures were not yet cut but held by an assistant, with moderate tension. It should be noted at this point that this tension was sufficient (as it later became apparent) to cause a partial rent in the tissues. Because of this, the sutures did not appear safe enough and, therefore, had to be reinforced later by a double suture over them. The entire separation of the carcinoma from the duodenum was then performed and the completely excised tumor could be removed. After the stomach cavity was cleaned with sponges and several bleeding arteries in the stomach wall were tied with fine (English No. 5) silk ligatures, the problem of the anastomosis between the considerably larger stomach lumen with the smaller opening of the duodenum arose.

"Inasmuch as it was desirable to avoid wedges and folds, the stomach walls themselves were sutured together first, beginning at the greater curvature namely from below until the remaining lumen of the stomach could be easily united with the opening of the duodenum. The closure of the stomach wall itself was performed with twenty-one silk sutures (stronger deep ones, alternating with fine superficial ones), the circular anastomosis between stomach and duodenum with 33 silk sutures in the same manner. By these 54 silk sutures, which were cut short, an exact union of the wounds was obtained because of the infolding of the wound edges and because only serosa and muscularis were included in the sutures. After superficially disinfecting the stomach again with 3 per cent carbolic acid solution, it was placed back into the peritoneal cavity and the abdominal wall, including the peritoneum, was closed by three plate sutures and, furthermore, several (7) deep and superficial silk sutures. No drainage. Carbolic acid gauze—compression bandage.

"During the operation, which lasted about one and a half hours, there was in the beginning both vomiting movements with partial prolapse of the intestines and a state of collapse. The blood loss was very little. The patient was placed in a warmed bed and covered with warm blankets. Temperature, 36.4 degrees; pulse could be felt but it was weak. After the patient had recovered she complained of a sensation of pressure in her stomach, no nausea, no vomiting or regurgitation. Comparatively well in the afternoon. The patient is taking only ice chips. Towards evening temperature 38.4 degrees, skin moist, pulse can be felt clearly, 110, gas is passing.

"*Specimen*. The shape of the extirpated tumor can be compared with a short bulky hunting horn and upon palpation it seems quite solid. The length at the greater curvature amounts to 14.5 cm. and the length at the lesser curvature to 10 cm. The circumference at the pyloric ring is 13.5 cm., the circumference of the rigid, wall-like opening toward the interior of the stomach is 22 cm. Beyond the duodenal extremity of the carcinoma there is still 2 cm. of normal duodenum to be seen on the specimen. At the pyloric ring the thickness of the carcinoma is 2 cm., more toward the stomach it is 1 cm., and finally at the cut margin,—the stomach wall is 0.5 cm. in thickness. A piece of omentum with some fat is attached to the lesser curvature. The anterior stomach wall is smooth on the outside, the posterior outer stomach wall shows, toward the lesser curvature, many groups of small gravel sized nodules. At the greater curvature close to the pylorus, two pea-size infiltrated lymph nodes can be seen. The lumen at the pyloric region is constricted rapidly so that at the pyloric ring only a larger sound can be passed. The mucous membrane is of a felt-like reticular appearance but shows no ulceration. The submucous tissue appears thickened and in it can be seen some hyaline sago-corn like spots. Microscopically the nature of the tumor is that of an infiltrating colloid carcinoma, mainly in the submucous tissue, whereas the mucous membrane shows only small celled infiltration and the glands atrophic. There are groups of carcinoma cells crowded in between the muscular bundles and they also spread into the subperitoneal connective tissue. The extirpated mesenteric lymph node shows the same structure, viz., colloid carcinoma.

"January 29: Two wine enemas (each 3 ounces) are retained. At night a small dose of morphine was injected because of some colic-like pain.

"January 30: The patient has had a good night's sleep and is feeling very well today. The lips show a more lively color. Some tenderness in the stomach region. Aside from ice chips she is taking every half hour to one hour a small tablespoon of sour milk which she likes and retains very well. In addition to that she is receiving a wine enema every three hours. Temperature 38.4 degrees, pulse strong —110. At three o'clock in the afternoon the patient is given a small amount of strong bouillon which she did not like and which stimulated regurgitation, therefore, it was not given to her again. The patient was of the opinion that the soup was too strong for her. Toward evening both gas and some liquid feces were passing. Temperature 39 degrees, pulse 120. At night a small dose of morphine was injected.

"January 31: The patient was sleeping quietly until morning. Temperature 38.4 degrees, pulse 110. Feeling well; the same medication is continued and besides there is peptone (English preparation) added to the wine enemas. (One teaspoonful of peptone dissolved in a small amount of luke warm water plus three ounces of wine.) The patient is praising again and again the pleasant effect of sour milk. Temperature in the evening 38 degrees, pulse 104. Toward midnight, soon after the last peptone enema, a fetid diarrhoeal evacuation of the bowels of considerable amount was taking place, accompanied by some pain in the abdomen; 0.01 gram of morphine subcutaneously injected; afterwards slept until morning.

"February 1: Patient feeling well, temperature 38.4 degrees, pulse 114. Instead of peptone enemas, three pure wine enemas were ordered for the whole day. Besides every hour one tablespoon of sour milk and ice chips repeatedly. At noontime, the attempt was made to give the patient a small amount of light veal soup (cooked without vegetables). But this soup too, was followed by regurgitation and because of this it was not given again. Mild bed sore in the sacral region—application of citric acid—boracic ointment. Temperature in the evening was 38.4 degrees, pulse, 110. Because of sleeplessness at night, a small dose of morphine was injected.

"February 2: Feeling well, patient considerably recovered, temperature 38.4 degrees, pulse 112. Two pancreas enemas (about 100 grams of fresh pancreas crushed by machine into a pap added to 1/5 liter of wine, one yolk pressed through a sieve to be used for two enemas). The patient is placed on a water filled mattress. Ointment treatment of the bed sore. After the second enema, diarrheal evacuation of the bowels is taking place, therefore, a return to pure wine enema is ordered. Temperature in the evening 38.2 degrees, pulse 102. Small dose of morphine injected.

"February 3: Feeling well, temperature 38.4 degrees, pulse 100. A wine enema in the morning is retained well. Besides, the patient is getting a few spoons of black tea and a little orange juice. Evening temperature 38.2 degrees, pulse 102. Small dose of morphine injected.

"February 4: *Wound dressing.* The wound looks dry and healed without any inflammatory reaction. Two plates are being removed (excluding the one in the middle) as well as most of the sutures. Carbolic acid gauze bandage. Patient feeling well. The previously yellowish color and bloated looking face has changed into a more normal looking but pale appearance. Temperature 38 degrees, pulse 100. Several spoonfuls of coffee and tea are tolerated well, light milk diet, wine enemas every 3 hours. Temperature in the evening 37.6 degrees, pulse 98. Small dose of morphine injected.

"February 5: *Wound dressing.* Removal of the third plate and the remaining sutures. Wound completely healed. The patient is taking several spoonfuls of milk and coffee. At noontime, eight spoonfuls of chicken broth (without vegetables) with yolks in it which she did like to take. In the afternoon she was taking half a cup of cocoa in milk (one teaspoonful of cocoa added to one cup of milk) which she also enjoyed. In the evening several teaspoonfuls of tea. Patient feeling very well. Morning temperature 37 degrees, pulse 98. Evening temperature 37.8 degrees, pulse 100.

"February 6: Temperature 37 degrees, pulse 90. Feeling well. Pap-like stools after a wine enema; half a cup of coffee. At noontime bouillon with eggs. In the afternoon cocoa in milk. In the evening a cup of tea. Iodoform powder on the bedsore at the sacral region. Temperature 38 degrees, pulse 92. Small dose of morphine injected.

"February 7: Temperature 38.4 degrees, pulse 114. The patient is doing well. Some pain in her lower abdomen which she thinks is due to her expected period. No meteorism, no pains in her upper abdomen. Slight increase of perspiration and thirst. (Ice chips and lemonade). Tea and milk for breakfast was taken with good appetite. At noontime chicken puree soup which appeared to her to be a little too strong and which she did not like to take very much. She did not like the apple compote offered. Gas and pap-like stools are passing. Towards evening start of menstruation. Temperature 39 degrees, pulse 120. Feeling very distended and very apprehensive; 0.01 gram morphine subcutaneously caused sedation and sleep. Before this, knotty stools and gas were passed. A rectal tube introduced. Gas passing again. Patient had a quiet night.

"February 8: Temperature 37.8 degrees, pulse 98. Patient feeling well again. Tongue moist, not coated but showing some tender rhagades. Appetite good. At noontime chicken broth with yolk, plum compote; in the afternoon tea and sweet biscuit; in the evening a cup of milk, afterward two large glasses of lemonade. Temperature 37.6 degrees, pulse 100. Small dose of morphine injected again.

"February 9: Temperature 37.4 degrees, pulse 98. Feeling well. Some knotty stools passed. In the morning plain milk, later on tea, at noontime chicken puree soup with yolks and plum compote (to which she said she would like to have some milk added). Two wine enemas per day. In the afternoon restlessness and colic-like pains with hot flashes alternating with chills. Finally a considerable amount of dry yellow knotty stools was eliminated. After a camomile enema, improvement. Temperature 39 degrees, pulse 98. Small dose of morphine injected. Lemonade.

"February 10: Temperature 37.4 degrees, patient feeling much better again. In the morning a cup of coffee, 1 hour later tea, biscuit. At noontime sago soup (she does not care for chicken puree because she thinks it is too strong for her). The bed sore scab is beginning to fall off under iodoform powder treatment. The patient has been lying in bed usually on her side and after one camomile enema with oil (to dissolve scybala) she eliminated once at noontime and again in the evening a considerable amount of stools of normal consistency. In the afternoon, one cup of coffee, tea in the evening. Temperature 38.4 degrees, pulse not above 100.

"February 11: Feeling well. Temperature 37.2 degrees, pulse 98. Coffee, milk, tea and biscuits. Grit soup with yolks, sherbert, 4 spoonfuls of wine (in 24 hours), coffee in the afternoon and milk, raspberry juice. Temperature in the evening 38 degrees, pulse around 100. Tea with biscuit and milk. Camomile enema, small dose of morphine injected. Her bed sore is treated from now on with silver

nitrate ointment instead of iodoform because there is fear of resorption of iodine.

"February 12: Coffee. Temperature 37.4 degrees, pulse 92. Yellow stools of normal consistency. Noodle soup with egg, wine, coffee, tea. Temperature 37.6 degrees, pulse 98.

"February 13: Same diet plus brains with eggs. Considerable amount of pap-like stools. Feeling well. Evening temperature 37.2 degrees.

"February 14: Temperature 36 degrees; pulse 90. Patient feeling very well, considerable amount of brown thick pap-like stools. On the right margin of the bed sore, over the sacral region, there is a cavity 1 cm. deep which is packed with iodoform and silver nitrate over it. Wine foam with biscuits and chicken soup (which she liked very much), coffee, in the evening chicken again and tea. Temperature 36.6 degrees, pulse 90.

"February 15: No fever, pulse around 90. At noontime half a chicken; in the evening ham. After camomile enema, pap-like stools. From now on the patient is taking a bath every day.

"February 16: Feeling very well. Grit soup, breaded chops with rice, wine (in addition pea puree from home). For the last few days a solid mass could be palpated (infiltration) in the stomach region which was not painful at all and has become considerably smaller already.

"February 17: No fever, pulse around 90. Noontime soup with egg, half a fried chicken, milk-rice, coffee, tea, ham, wine, biscuit. In the evening fried veal; stools normal. A part of the bed sore scab was cut off with a pair of scissors.

"February 18: Feeling very well. Soup and chicken. No stools; camomile enema.

"February 19: Knotty stools; at noontime beefsteak with spinach. At night colic-like pains in the stomach most likely due to nervous excitement inasmuch as the patient wants to go home under any circumstances. Small dose of morphine injected; good night's sleep.

"February 20: Normal stools twice. At noontime stuffed pigeon with compote. The patient's weight is 39.36 kilograms. The patient is discharged due to her urgent pleas. The status of the patient at the time of discharge is as follows: The color of her face is still pale, however, a little color is returning to her cheeks. The lips show a vivid color and the bloated expression of the face has disappeared. Tongue very clean and not at all coated. The abdomen appears a little larger than before, the incision on the abdominal wall is dry and healed and directly under it one can feel the infiltrated hard region which had been larger before and is now smaller and apparently represents the stomach sutures at the greater curvature. No pains on palpation. At the lower part of the sacral region, a hazel nut size bed sore can still be seen in which the tissue down to the fascia of the muscle is missing. The necrotic part of the tissue had been cut off with the scissors and one can see now not too active but healthy looking granulations. For 8 days the patient has been lying only on her side in bed in order to speed the healing of the bed sore. Temperature and pulse were normal; the patient has not been out of bed, yet she is being brought home on a stretcher to her apartment: VIII. Landrengasse 41, (second floor).

"*Follow-Up Notes* (*Private Practice*). February 25: Patient feeling well, no complaints of any kind. Normal stool daily, no enema needed. Sleeping well without injection; a bath twice a week. As regards the diet, the patient is taking coffee in the morning, later on ham or beer with bread and butter and wine. At noontime, soup, beefsteak or roast fowl, pigeon or chops with some vegetables (spinach) and dessert (milk-rice, etc.) In the afternoon, coffee, in the evening roast meat. Since yesterday the patient is drinking malt beer (Hoff) at noontime which she enjoys very much. Treatment of bed sore with silver nitrate ointment 1%. No iodoform. The granulations are progressive while the size of the wound has not become smaller yet.

"March 2: Further recovery of the patient, temporarily she is out of bed, sitting in an armchair or walking around a few steps. Appetite good, same diet, normal stool daily without enemas. If she takes larger quantities of food than usual she has a feeling of tension in her stomach. Bed sore showing luxurious granulations. Sleeping very well.

"March 3: After one abundant meal (and cold apple strudel) partial vomiting of the meal took place but the next day she was feeling well again.

"March 8: Patient well; vomiting has not recurred. The bed sore has become much more shallow.

"Recurrence. Death 4 months after the operation. (Carcinoma of the stomach and omentum.)

"Necropsy was performed upon the patient and diffuse hepatic and omental metastases found. The stomach had become somewhat dilated but the anastomosis with the duodenum was patent."

The next two partial gastrectomies that Billroth performed were surgical mortalities. One died on the eighth day and one on the evening of operation. The early experiences with partial gastrectomy for carcinoma were discouraging indeed and for years there was serious discussion as to whether the operation was worthwhile.

REVIEWS OF NEW BOOKS

THE new second edition of Hauser's *Diseases of the Foot*[1] is a well written and valuable contribution to the library both of the orthopedic surgeon and the general practitioner. To one who has often read with dismay descriptions of some of the drastic operative procedure recommended in contributions and textbooks on orthopedic surgery, and who has wondered how so finely constructed and complicated a structure as the foot could ever be the same after undergoing the treatment suggested it is both assuring and impressive to read of the conservative treatment recommended for so many of the conditions described in this monograph—treatment where success is amply attested in the author's practice.

Of the very complete presentation of every phase of abnormal conditions affecting the foot—congenital deformities, injuries involving the bones, joints, ligaments, tendons, nerves; chronic and acute inflammations; tumors; pathological entities of uncertain origin, such as Sudeck's atrophy, Koehler's disease and Freiberg's disease—two chapters are of particular interest and importance, chapter 5 on Pes Valgoplanus (Flatfoot) and chapter 11 on Talipes (Clubfoot). The clearly described and well illustrated description of the conservative treatment which the author has described and successfully carried out in these conditions must recommend itself to every surgeon who is faced with similar problems. Chapter 4 on Hygiene and General Care, and the concluding chapters (27–30)—Technique of Local Anesthesia, Special Techniques in the Care of the Feet, Technique for Manipulation of the Foot and Orthopedic Appliances for the Foot—contain many practical suggestions every young surgeon in particular can read with profit. SUMNER L. KOCH.

THE sixth edition of *Die gynaekologischen Operationen und ihre topographisch-anatomischen Grundlagen*[2] by Heinrich Martius, director of the Frauenklinik at the University of Gottingen, was published in 1950. This volume of 422 pages covers the field of gynecological surgery with varying degrees of aptitude. Also included are short discussions of some phases of abdominal surgery with which the gynecologist should be familiar. The illustrations by Frauleins, Droysen, and Hartmann are for the most part excellent.

The volume is arranged with the first and second sections making up about three-quarters of the entire edition and covering abdominal and vaginal procedures. The third section is devoted to a very lengthy discussion of urinary incontinence and its treatment. Curettage of the uterus is covered in the fourth section. Finally the fifth and sixth sections describe the general surgical procedures mentioned. Preoperative and postoperative care and anesthesia are given only occasional and brief consideration. References to literature are conspicuous by their infrequency.

Under section 1, there are excellent illustrations and discussion of the anatomy of the abdominal wall and procedures of opening and closing the abdominal incision including the Pfannenstiel incision. Two fine, diagrammatic sketches of the pelvis and its contents follow. The discussion and illustrations of abdominal hysterectomy, both total and subtotal, are superb and detailed enough so that one should be able to follow the steps without difficulty. The procedure described is very similar to that used generally in this country. The old argument of total versus subtotal hysterectomy is adequately discussed with little mention, however, of the possibility of increased morbidity in total hysterectomy in the hands of the more poorly trained individual. The mortality figures mentioned in the text are in general higher than those recently quoted in the United States. The figures quoted vary from 1.3 to 1.9 per cent for subtotal and from 3.6 to 7.8 per cent for total. The incidence of carcinoma of cervical stump of 0.3 to 0.4 per cent agrees with usual statistics in this country. Again the sketches and discussion of myomectomy are well done. The Wertheim procedure is covered in lengthy discussion and illustrations both natural and schematic and particularly of the relationships in the operative area are extremely well done. There is a short discussion on the plastic procedure of Strassmann for developmental anomaly of the uterus.

Tubal pregnancy is fully discussed with diagnostic procedures, and treatment, both medical and operative, is covered in the text. Culdoscopy which is now well established in this country as a diagnostic aid in early unruptured cases is not included. Adnexal disease, both inflammatory and neoplastic, is given brief but adequate treatment in the succeeding 35 pages. Plastic operations on tubes for sterility are discussed very briefly. Tubal insufflation (Rubin's test) is not included in the discussion nor elsewhere in the text. A lengthy section which seems relatively out of proportion to other subjects is devoted to sterilization. The "inguinal sterilization," especially, is more than fully illustrated and explained in 15 pages. This inguinal approach is, of course, similar to the Alexander-Adams operation for suspension and has been a favorite in Germany for years although largely given up in this country. The latter operation plus several other suspension procedures are then briefly described. The author explains that

[1] DISEASES OF THE FOOT. By Emil D. W. Hauser, M.S., M.D. 2d ed. Philadelphia, London: W. B. Saunders Co., 1950.

[2] DIE GYNAEKOLOGISCHEN OPERATIONEN UND IHRE TOPOGRAPHISCH-ANATOMISCHEN GRUNDLAGEN. By Heinrich Martius. Stuttgart: Georg Thieme; New York: Grune & Stratton, Inc., 1950.

the Alexander-Adams procedure should not be used where there is intrapelvic pathology as a cause of or associated with the malposition. An interesting procedure of fixation of the round ligaments to the anterior surface of the fundus plus advancement of the bladder is well explained and illustrated. The first section closes with a very brief discussion of presacral neurectomy.

The second section opens with a discussion and excellent drawings, both schematic and natural, of the "simple vaginal hysterectomy." The only omission here is an explanation of closure in prolapse cases where techniques such as the Mayo and Chicago group employ are usually performed in this country rather than simple approximation. Vaginal subtotal hysterectomy, a procedure used here only in the Richardson Spaulding composite operation, is described in some detail. The illustrations for radical vaginal procedure for carcinoma of cervix are excellent.

In the discussion of vaginal myomectomy either x-ray or intrauterine radium therapy immediately following myomectomy is recommended for patients in the climacteric with additional myomas. This seems to be an unnecessary procedure, since it is very rare in our experience to have need for additional means to control bleeding, and if a further procedure is necessary we in general lean toward hysterectomy after any intrauterine infection has subsided. Cervical amputation and trachelorrhaphy are adequately discussed with excellent illustrations of the Emmet and Sturmdorf procedures. Minor cervical procedures, as knife biopsy, removal of polyps, and puncturing of cysts, are mentioned and are followed by brief descriptions of vaginal hysterotomy and posterior colpotomy.

A full discussion of vaginal plastic procedures is accompanied by adequate illustrations. The simple anterior colporrhaphy and the same procedure with advancement of the bladder are quite similar to the operations performed in most clinics in this country. Two vaginal procedures which seem to be designed to advance the bladder and suspend the retroposed fundi are briefly described. The Watkins-Wertheim-Schauta operation is adequately discussed and illustrated. An interesting procedure in which the uterosacral ligaments are cut, brought through the broad ligaments and sutured to the anterior surface of the fundus would seem to be useful in an occasional instance not only to aid in fixation of the uterus but also to eliminate the possibility of an enterocele. Abdominal fixation of the fundus for prolapse is mentioned.

There are several excellent illustrations of the muscular and fascial structures of the perineal floor followed by extensive pictorial handling of the perineorrhaphy and a good discussion. Description of the Le Fort operation is followed by a procedure designated as the subtotal colpocleisis of Labhardt. The value of the latter procedure is not entirely clear and does not seem to be as useful as the modification of the Le Fort by Goodall and Powers. The layer method for repair of third degree perineal tear is described but the Warren flap procedure, very useful in certain cases, is omitted. Rectovaginal and other perineal fistulas are illustrated diagrammatically and corrective procedures are briefly discussed.

Lesions of the vulva and vagina are discussed with very few inadequate words, and illustrations are confined to an adequate description of excision of a Bartholin cyst and to schematic drawings of the areas involved in surgery for carcinoma of vulva. Taussig's and McKelvey's recent greatly improved statistics for 5 year salvage with the radical procedure are not mentioned. This section closes with a scanty description of the formation of an artificial vagina.

Section 3 is certainly to me one of the outstanding features of this volume. The subject of urinary incontinence is handled in a most detailed fashion. The chapter begins with a lengthy discussion of fistulas and a classification based on method of treatment. There are schematic representations of the various types, followed by excellent natural drawings of steps in repair. The helpful Schuchardt incision is described. A detailed discussion of the mechanism of urination and of the structures involved is accompanied by numerous illustrations. The procedures for the cure of incontinence due to muscle deficiency include plication of the urethra and the so called "sphincter" region; the use of the gracilis or levator ani muscles as a urogenital diaphragm; the part played by the bulbocavernosus and its adjacent fat pad; and the Goebell-Stoeckel procedure. In the discussion of the latter, references are made to the work of Aldridge in America and Millen and Read in England. A procedure for formation of urethra is described. The chapter closes with a discussion of ureteral injuries, both immediate and late, and their treatment.

Section 4 is devoted to a discussion of dilatation of cervix and curettage of the uterus. Types of anesthesia are suggested, and the steps in the procedure are given in detail. An office procedure for preliminary dilatation of the cervix is described. Finally, a discussion of perforation and its sequelae is presented.

Sections 5 and 6 include general surgical procedures with which the gynecologist should be familiar. Repair of inguinal and femoral hernia is described in some detail, and other abdominal hernias are discussed. Intestinal resection, colostomy and appendectomy are well handled. The subjects of hemorrhoidectomy and excision of fissure-in-ano are briefly mentioned.

In conclusion this volume can be recommended especially on its treatment of the generally accepted abdominal and perineal procedures and the excellent handling of urinary incontinence. Its greatest inadequacies are found in the discussion of vulvar lesions and their treatment; the omission of technique for use of radium in treatment of carcinoma of cervix and fundus; and the relative absence of references to the literature. DONALD WOODRUFF.

IT is regrettable that J. Marion Sims cannot return to read and enjoy Seale Harris' biography[1] of "the father of American gynecology." The scholarly emeritus professor of medicine of the University of Alabama has done his utmost to portray an exhaustive, unbiased picture of Sims' life.

Marion Sims' autobiography, read by Harris at the age of fifteen while accompanying his father on his daily professional calls, aroused in him an interest in collecting information about Sims which has continued unabated throughout the years and has resulted in the publication of numerous notes and articles, climaxed by the present biography.

Marion Sims was born in 1813 near Lancaster, South Carolina, in which town he grew to manhood. The guiding light of his entire life was his childhood sweetheart, daughter of a socially prominent Lancaster physician whose family tried to thwart the romance which eventually culminated in marriage.

Other details of Sims' early years seem unimportant, and they did not in any way indicate any particular ability or ambition. At seventeen, when he left home to attend Carolina College at Columbia, South Carolina, he was a frail fellow of one hundred and eight pounds and was quite devoid of confidence in himself or hope in his future.

Two years of unconcerned drifting through college were followed by a decision to be a doctor, not because of any leaning in that direction, but because he could not bear the thought of becoming a preacher or a lawyer. Then, after unprofitable months in a doctor's office and a three months' course of lectures at Charleston Medical School, he entered Jefferson Medical College in Philadelphia, in 1834.

At Jefferson, stimulated by the enthusiasm and example of Dr. George McClellan, he became convinced that his career must be surgery. At this time, he still had a marked lack of confidence in his own abilities and was horrified at the thought of writing papers or making speeches, despite his classmates' recognition that he had a natural aptitude as a convincing and forceful speaker.

Upon graduation from Jefferson, without any further experience and with practically no medical training and almost no knowledge of medicine, there followed a brief discouraging period of practice in Lancaster. Then came a long trek to the much heralded, newly opened pioneer country of Alabama, where Sims located in the little settlement of Mount Meigs, about twenty miles east of Montgomery. After establishment of a practice in that malaria infested country, he married his childhood sweetheart, Theresa Jones.

Four years later, despite an otherwise happy life, chronic ill health finally forced the Simses to move. This time it was to Montgomery, then a town of 4,000 inhabitants.

In Montgomery, Marion Sims entered upon the epoch-making work which led to his world renown. Early operations were on cases of strabismus, clubfeet, and harelip. It was only after he was urgently advised by Dr. Silas Ames, Montgomery's medical leader, that he began to publish reports of his operative work in the *American Journal of Medical Sciences* and thus became more widely known to the medical profession.

Sims' work on vesicovaginal fistula marks an epoch in the history of American medicine. But, although he became world famous in his time, the story of his struggles and disappointments preceding the development of a successful fistula operation is now so forgotten that even eminent specialists in gynecology tend not to be conversant with the essential features of his work.

Hope that he might cure vesicovaginal fistula had been inspired in Sims by recognition of the fact that air rushing into the vagina upon attempted replacement of the malposed organs might also be helpful in making the vaginal walls visible. It occurred to him that an instrument might be more serviceable than fingers in aiding such exposure and for that purpose he purchased a pewter spoon. With the patient on her knees, her head in the palms of her hands, and two students pulling lateralward at the vaginal orifice, introduction of the bent handle of the spoon was accompanied by an inrush of air and dilation of the vaginal cavity with resultant excellent exposure of the fistulous opening and adjacent tissues.

The evolution of a satisfactory posture and an instrument for exposure resulted in the development of the Sims position and the Sims speculum. Now chiefly of historical interest, the Sims position is obtained by placement of the patient on the left side and chest, the right knee flexed, the thigh drawn up, the left arm laid posteriorly along the back. The Sims speculum continues to be a useful instrument. As at first perfected and employed, it was made of German silver, had a seven inch handle and a bent, two and one-half inch concave highly polished vaginal end. Illumination was obtained by use of a mirror and reflected sunlight.

Sims figured that all that now remained to be done to cure the patient was to close the opening and keep it closed. A small private hospital, which had been built in the yard of Sims' home because he needed a place to care for the numerous slaves who were being sent to him as patients, was now doubled in capacity to sixteen beds, and a surgical fight to cure vesicovaginal fistula was begun in December, 1845. Three colored patients, Lucy, Betsy, and Anarcha, became famous as Sims' first fistula cases.

This was in the days before anesthesia. The only sedative used was powdered opium.

Sims' early operative attempts, with silk employed as suture material, invariably resulted in failure. Finally the use of silver wire, drawn out to horsehair thinness brought success.[2] The sutures, when placed

[1] WOMAN'S SURGEON; THE LIFE STORY OF J. MARION SIMS. By Seale Harris, M.D., with the collaboration of Frances Williams Browin. New York: The Macmillan Co., 1950.

[2] Whether Sims merits credit for introduction of silver wire as suture material is open to question. At any rate, he did popularize it as the most uniformly successful suture material then extant.

were passed through strips of lead to prevent cutting; the ends were threaded on perforated bird shot and pulled tight before compressing the shot with forceps. A retention catheter was kept in place until removal of the sutures, one week after operation. (It may be noted that mobilization of the bladder, to allow relaxation around the fistula, the cardinal feature in present-day fistula operations, was not thought of at that time).

Anarcha was the first to be cured of her fistula, after a series of thirty operations performed without anesthesia at irregular intervals throughout a period of three and one-half years from December 1845 to May, 1849. The use of silver wire sutures was the final factor which led to success.

Lucy and Betsy had likewise been subjected to an interminable series of operations during the same period of time and were also finally cured after success with Anarcha. All of this work was conducted in Sims' private hospital, at his own expense, after dogged and determined effort, and after all of his medical confreres had long since become convinced that he was wasting his life in fruitless effort.

Such was the experience of Sims in learning to cure vesicovaginal fistula. Throughout the years of repeated surgical disappointment, there had been worry over finances, and after success with the technique of the fistula operation there ensued a protracted period of ill health, chiefly chronic diarrhea, which Harris, with his present day knowledge of internal medicine, ascribes to bacillary dysentery complicated by vitamin deficiency.

A search for health became a dominant problem with Marion Sims. He also had a restless nature and an unusual craving for wide social contacts and professional recognition. Perhaps all of these factors entered into a decision to move to New York, which he had many times visited during his four year odyssey in search of health. So we find him in New York, in 1853, faced with another discouraging period of ill health, trial, and adversity.

Despite success with cases of vesicovaginal fistula, Sims had only a limited acquaintance and little reputation in New York. He met with some early limited success in demonstration of his fistula operation but soon learned that others were profiting from his ideas and technique without giving him recognition or furthering his ambition to gain a foothold.

Then there came to Sims the idea of establishing a hospital, exclusively for women, which would enable him not only to gain a foothold in New York but would also fill a very great need. Despite financial worries and ill health, he began making the rounds of New York's leading physicians, telling them of his ideas and asking their advice as to ways and means of creating a special hospital for the treatment of diseases and physical troubles peculiar to women.

Sims' hospital idea was a forlorn hope until he found Henri Luther Stuart, whom he met through an old neighbor and patient from Montgomery. Stuart, a rare character, was a successful and altruistic man, interested in all sorts of problems and activities. He listened to Sims' story and was immediately ready with a plan. He proposed that Stuyvesant hall be rented for a meeting for the whole medical profession to hear an address by Sims on the need for a hospital for the treatment of the diseases of women. He proceeded to carry out the idea. Trips were made to various newspaper offices, where he exhibited the embarrassed Sims and made arrangements for publication of notices announcing the forthcoming meeting. This was advertising in every respect except that it was not paid for. It made Sims wince but he was desperate, so he agreed and began preparation of the address he was scheduled to deliver. At the well attended meeting, Sims told graphically of his experiences in his little hospital in Montgomery, where he had sought and found a solution of the tragedy of vesicovaginal fistula and other disabilities of women. He next presented his view that New York needed a hospital for women, and he then sat down. An embarrassing silence followed. As he had hoped, many eminent medical men who were present were favorably impressed and finally rose to express their views. Sims was commended very heartily by various speakers and a vote of thanks was passed for his presentation of the hospital project. Thereupon, the chairman was empowered to appoint a committee to carry out Sims' plan for the establishment of a woman's hospital.

Thereafter began an ardent and prolonged campaign, with Sims the motivating and determined spirit, which finally eventuated in establishment of the Woman's Hospital, the institution in which he later attained such renown and in which he helped to develop the specialty of gynecology. It was truly a Herculean task and was accomplished by a stranger in New York, aided, it is true, by the quite remarkable Henri Stuart and others, notably Mrs. Thomas C. Doremus.

It was his untiring efforts in founding the Woman's Hospital which redound to Sims' credit and lasting fame more than all else in his life of unusual accomplishments.

The first Woman's Hospital, a rented four-story building at 83 Madison Avenue, opened in 1855. Sims took part, also, to a lesser extent, in the building of the more permanent Woman's Hospital located where the New York City's potter's field had been and which is now the site of the Waldorf-Astoria Hotel. Sims' promise that twenty-five beds would be permanently set aside for the use of the city's poor was a factor in overcoming firmly rooted opposition to the city's gifts of the land on which the hospital was to be built.

Marion Sims was a man of finely chiseled features, possessed of remarkable personal charm and magnetism; yet he had many faults and made many mistakes. He was impulsive and had a volatile temperament. He was beyond reproach in his family life. He greatly enjoyed giving extravagant brilliant parties, featuring an abundance of food and drink, yet his own life was one of simplicity. He kept regular

hours, ate very temperately, avoided alcohol and tobacco and even tea and coffee.

Sims was an exceedingly graceful, rapid operator. Speed in operating meant much in those preanesthetic days, quite as much as does deft and accurate work at the present time. Thomas Addis Emmett, his famed successor, remarked on Sims' dexterity, his boldness and self-reliance, his unequalled ingenuity. "He was so fertile in resource when I first knew him that he perfected scarcely a tithe of the brilliant conceptions passing through his mind, and it was impossible to see him perform even the most simple operation without learning something new."

Seale Harris' story describes in detail Sims' rise to fame in New York; his many trips to Europe; his operations in foreign clinics and acclaim as surgeon to royalty in various countries. (At that time his name had become a household word, his every move a topic for newspaper comment.)

Other notable details in the life of this remarkable man include his service as chief of the American Ambulance Corps in the Franco-Prussian war and his decoration for that service with the French Legion of Honor; his return to New York and his bitter denunciation of the Governors of the Woman's Hospital, followed by their acceptance of his resignation as surgeon; his election shortly thereafter in 1875 as President of the American Medical Association; in 1880, his election as President of the American Gynecological Society, of which society he was a founder member; his reinstatement in the same year as Consulting Surgeon of the Woman's Hospital; his contributions not only to gynecology but in the field of abdominal surgery, notably gall-bladder surgery, in which he was a pioneer; his textbook, *Clinical Notes on Uterine Surgery*, and a great many other original papers.

We must forgive Seale Harris if he evinces hero worship in this book. It is not likely that he magnifies Sims' virtues and his ability, but there is a tendency to gloss over many mistakes and faults which were often dominant in the life of this pertinacious, gifted, and remarkably magnetic man. All in all, it is a fine story, extremely well written, and one of which the author may be justly proud.

ARTHUR H. CURTIS.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

EL INJERTO DE VENA CON TUBOS DE VITALIUM PARA REEMPLAZAR AORTA, URÉTER Y COLÉDOCO. By Elberto Cabanzo Cabanzo. Bogotá: Universidad Nacional de Colombia Seccion de Extension Cultural, 1950.

TREPHINE TECHNIQUE OF BONE MARROW INFUSIONS AND TISSUE BIOPSIES. By Henry Turkel, B.A., M.A., M.D. 4th ed. Detroit: Gale Printing Co., 1950.

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ATLAS DER NORMALEN HISTOLOGIE UND MIKROSKOPISCHEN ANATOMIE DES MENSCHEN. By E. von Herrath and S. Abramow. Stuttgart: Georg Thieme; New York: Grune & Stratton, Inc., 1950.

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HEPATOSTOMIA. By Atilio J. Lasala and Manuel Jose Vazquez. Prologue by Professor Ricardo Finochietto. Buenos Aires: Lopez & Etchegoyen, 1950.

PHYSIOLOGY OF SHOCK. By Carl J. Wiggers, M.D., Sc.D., F.A.C.P. New York: The Commonwealth Fund, 1950.

YOUR PROSTATE GLAND; LETTERS FROM A SURGEON TO HIS FATHER. By Reed M. Nesbit, M.D. Springfield, Ill.: Charles C Thomas, 1950.

THE LIFE AND TIMES OF GASPARE TAGLIACOZZI; SURGEON OF BOLOGNA, 1545–1599 WITH A DOCUMENTED STUDY OF THE SCIENTIFIC AND CULTURAL LIFE OF BOLOGNA IN THE SIXTEENTH CENTURY. By Martha Teach Gnudi and Jerome Pierce Webster. New York: Herbert Reichner, 1950.

MONOGRAPHS ON SURGERY 1951. Edited by B. Nolan Carter, M.D., Ph.D. New York, Toronto, Edinburgh: Thomas Nelson & Sons, 1950.

REST AND PAIN. By John Hilton, F.R.S., F.R.C.S. Edited by E. W. Walls, M.D., Ch.B., B.Sc., and Elliot E. Philipp, M.A., M.B., B.Chir., M.R.C.S., M.R.C.O.G., in collaboration with H. J. B. Atkins, D.M., M.Ch., F.R.C.S. Philadelphia, London, Montreal: J. B. Lippincott Co., 1950.

ATLAS OF HISTOLOGIC DIAGNOSIS IN SURGICAL PATHOLOGY. By Karl T. Neubuerger, M.D. With a section on Exfoliative Cytology. By Walter T. Wikle, B.S., M.S., M.D. Photography by Glenn E. Mills, B.A., M.A. Baltimore: The Williams & Wilkins Co., 1951.